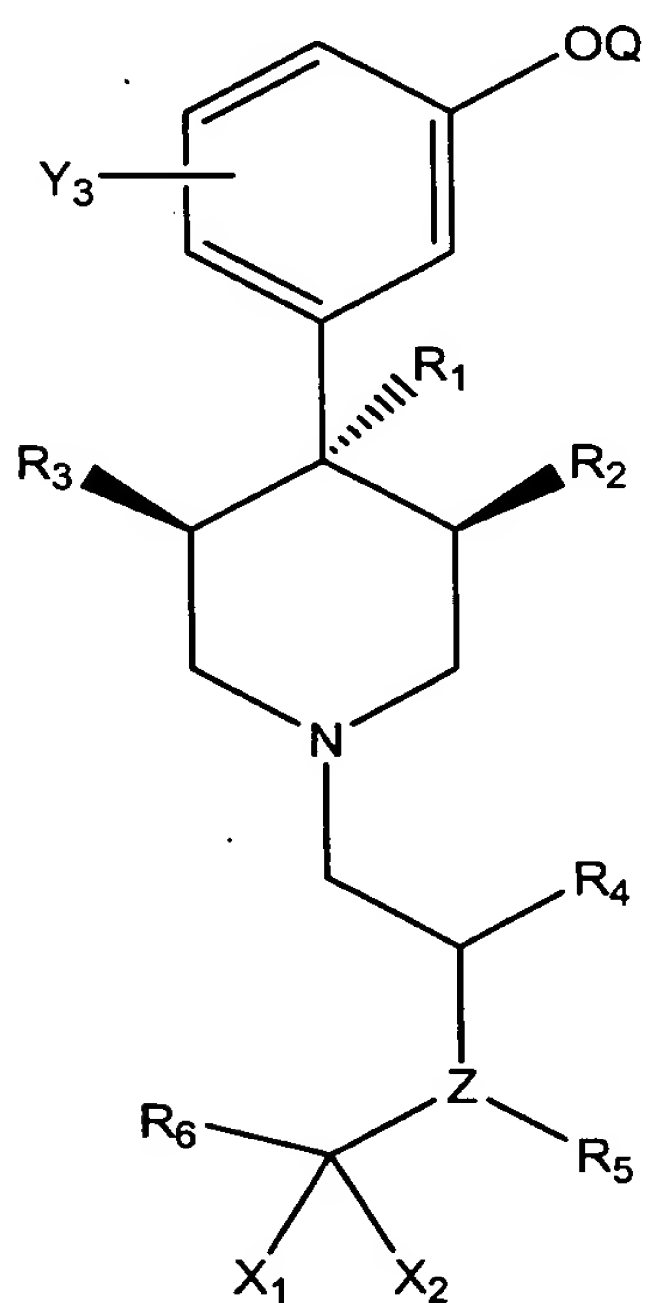


CLAIMS

Please amend the claims as follows:

Claim 1 (Currently Amended): A method of binding a kappa opioid receptor in a subject in need thereof, comprising:

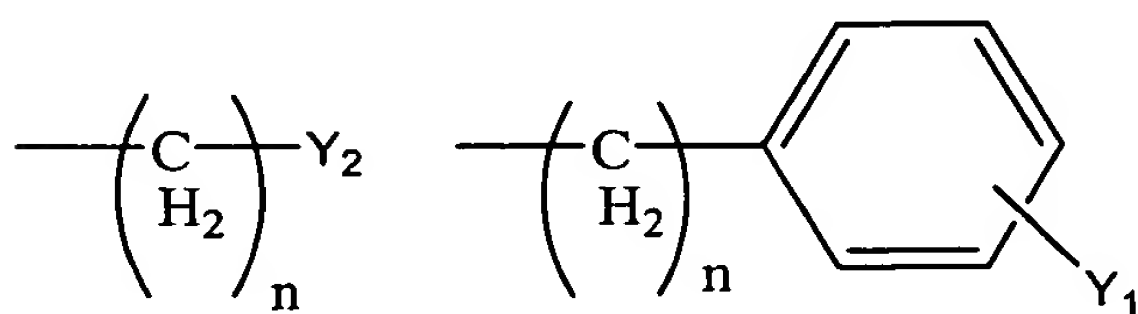
administering to said subject a composition comprising a kappa opioid receptor antagonist and a physiologically acceptable carrier, wherein the kappa opioid receptor antagonist is a compound of formula (1):

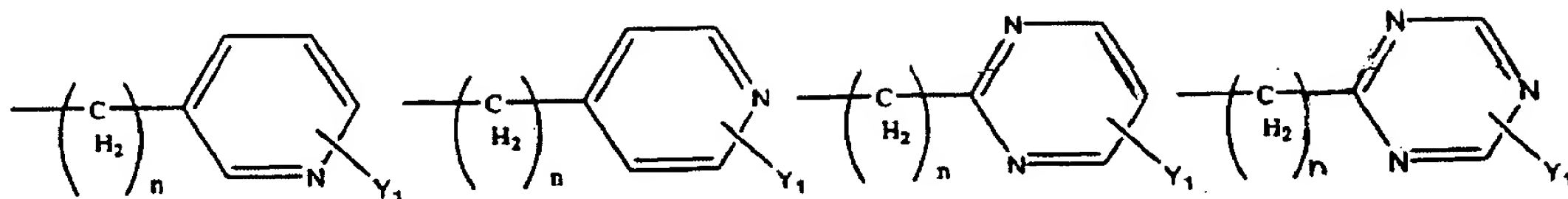


(I)

wherein Q is H or COC₁₋₈ alkyl;

R₁ is C₁₋₈ alkyl, or one of the following structures:





Y_1 , is H, OH, Br, Cl, F, CN, CF_3 , NO_2 , N_3 , OR_8 , CO_2R_9 , C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, or $CH_2(CH_2)_nY_2$;

Y_2 is H, CF_3 , CO_2R_9 , C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, CH_2OH , CH_2OR_8 , or $COCH_2R_9$;

Y_3 is H, OH, Br, Cl, F, CN, CF_3 , NO_2 , N_3 , OR_8 , CO_2R_9 , C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, or $CH_2(CH_2)_nY_2$;

R_2 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl or CH_2 aryl substituted by one or more groups Y_1 ;

R_3 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl or CH_2 aryl substituted by one or more groups Y_1 ;

wherein R_2 and R_3 may be bonded together to form a C_{2-8} , alkyl group;

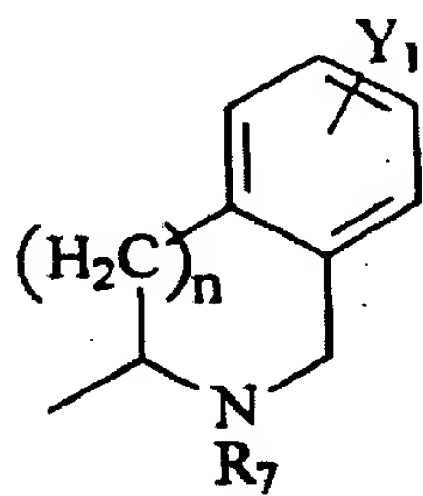
R_4 is hydrogen, C_{1-8} alkyl, CO_2C_{1-8} alkylaryl substituted by one or more groups Y_1 , CH_2 aryl substituted by one or more groups Y_1 or CO_2C_{1-8} alkyl;

Z is N, O or S; where Z is O or S, there is no R_5

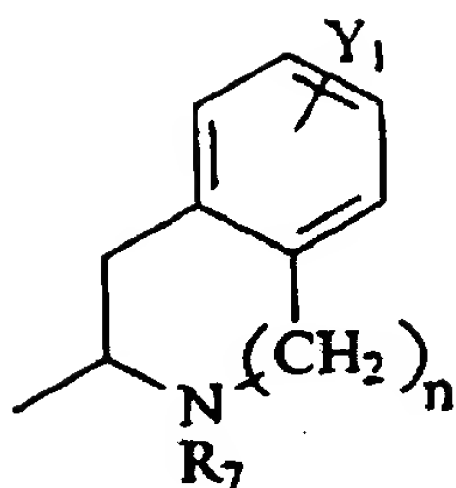
R_5 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, $CH_2CO_2C_{1-8}$ alkyl, CO_2C_{1-8} alkyl or CH_2 aryl substituted by one or more groups Y_1 ;

n is 0, 1, 2 or 3;

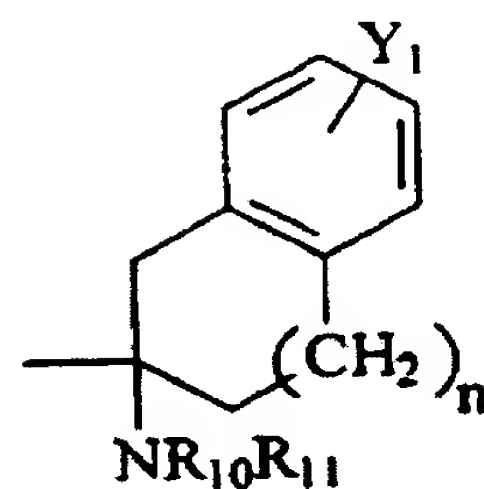
R_6 is a group selected from the group consisting of structures (a)-(w) and (cc)-(bbb):



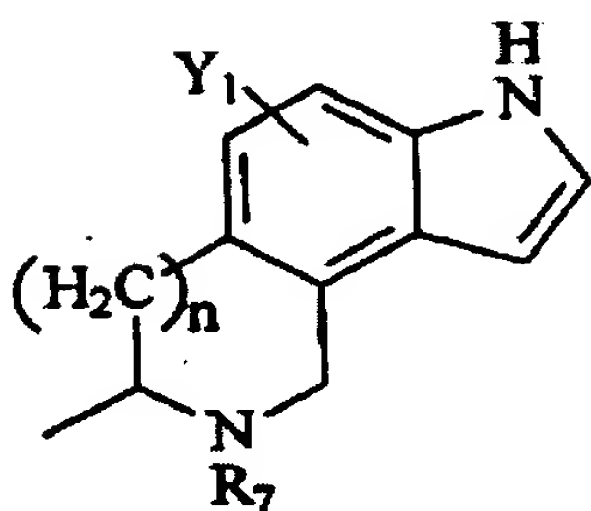
(a)



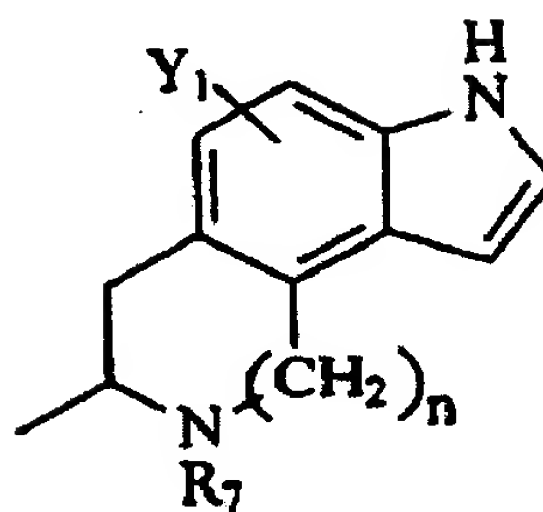
(b)



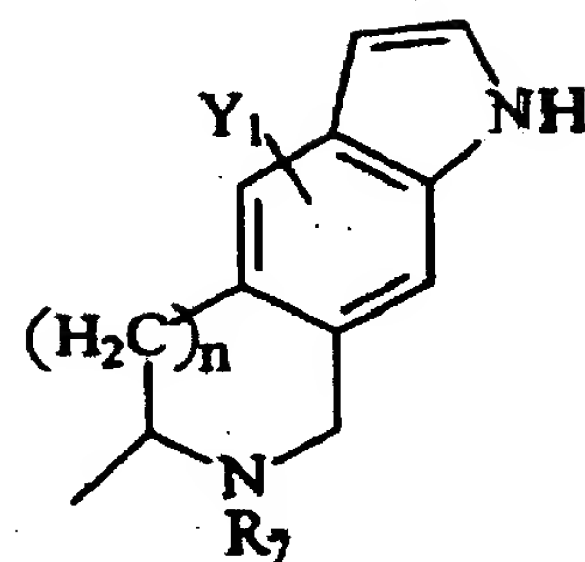
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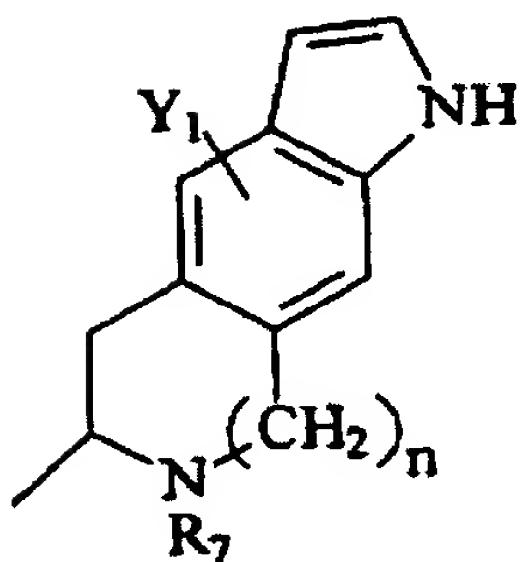
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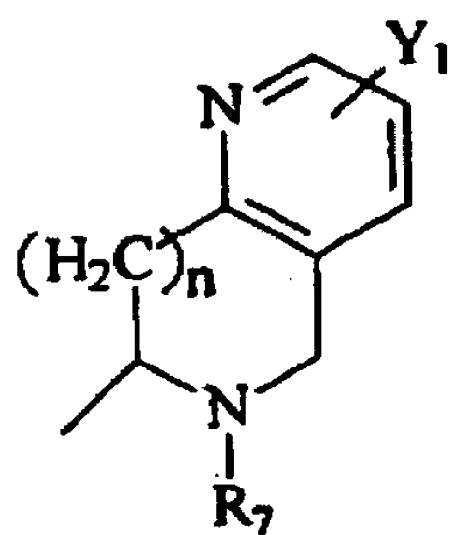
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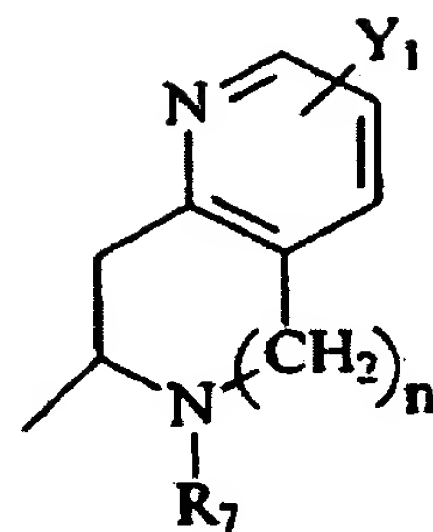
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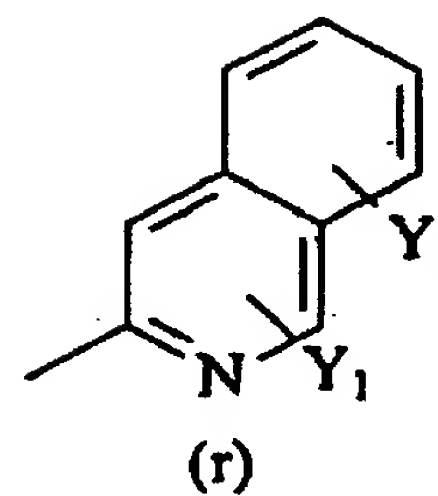
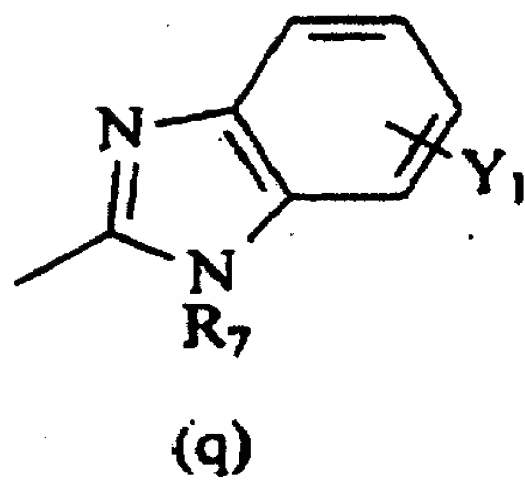
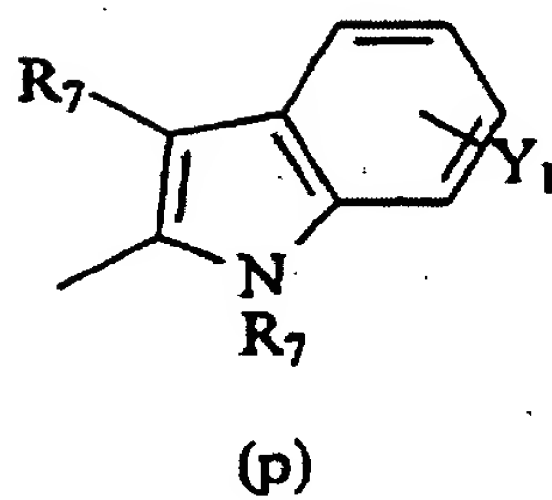
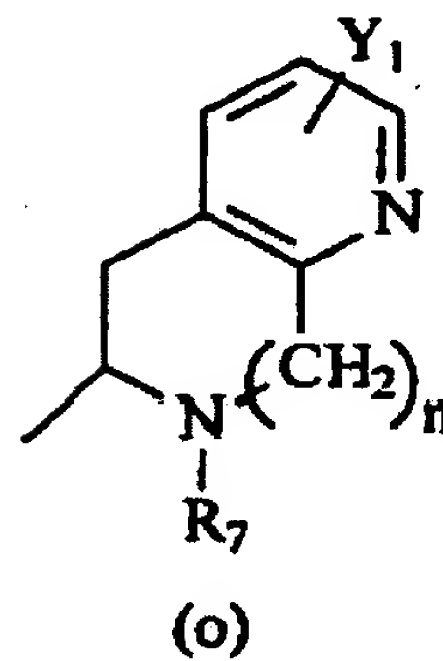
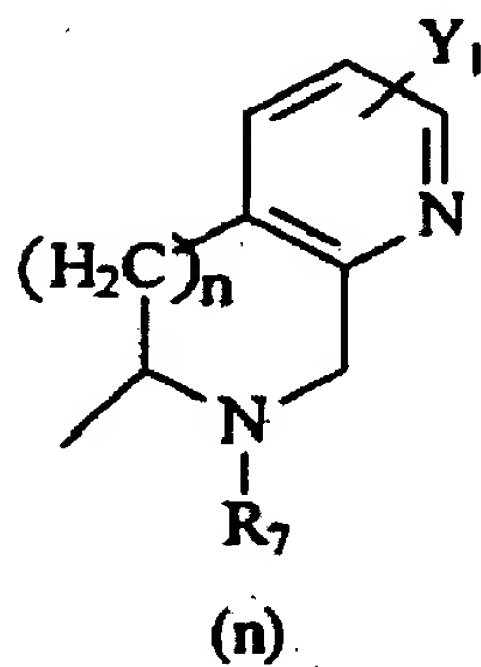
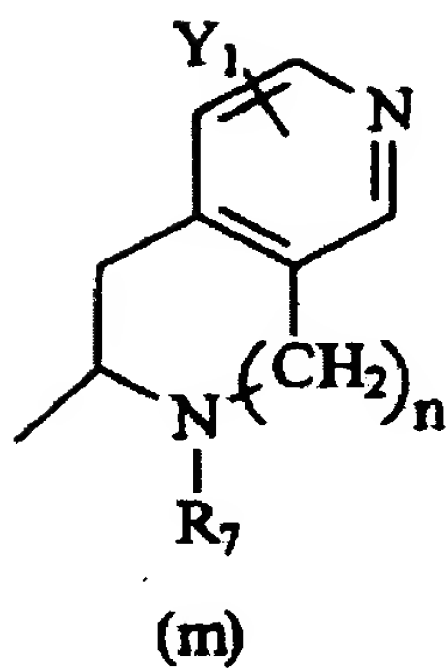
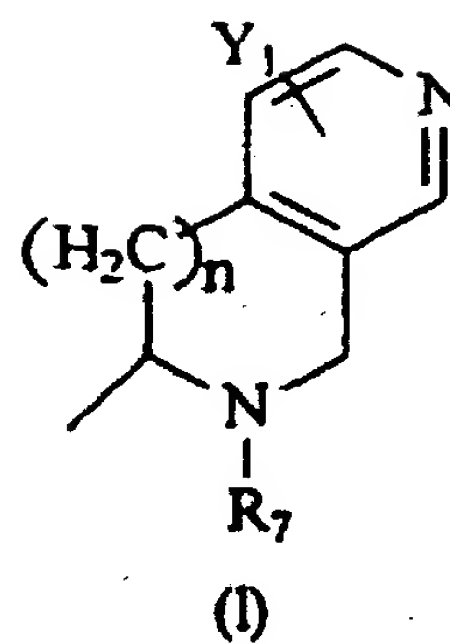
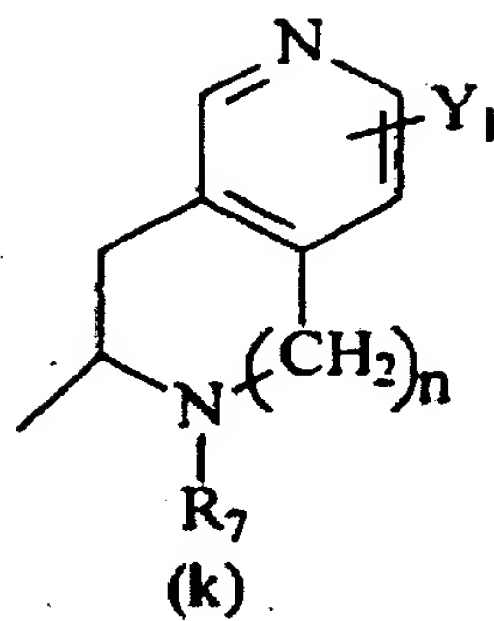
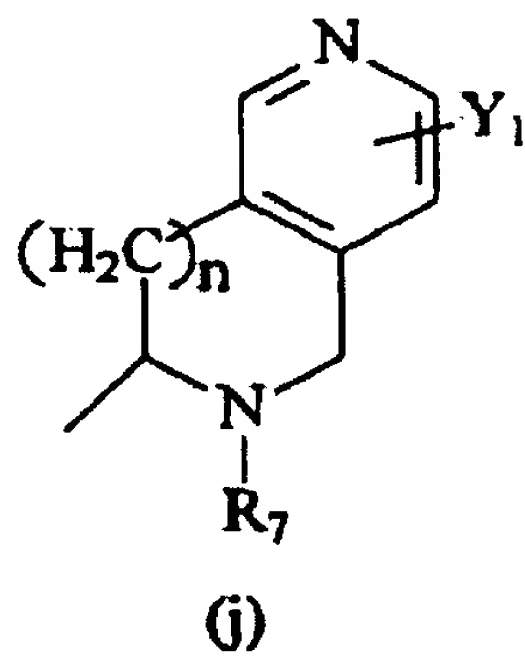
(g)

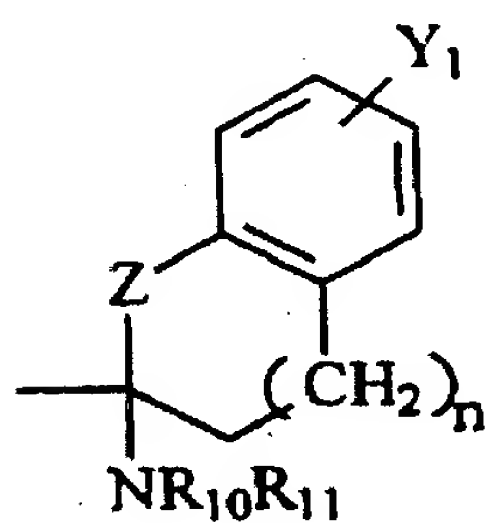


(h)

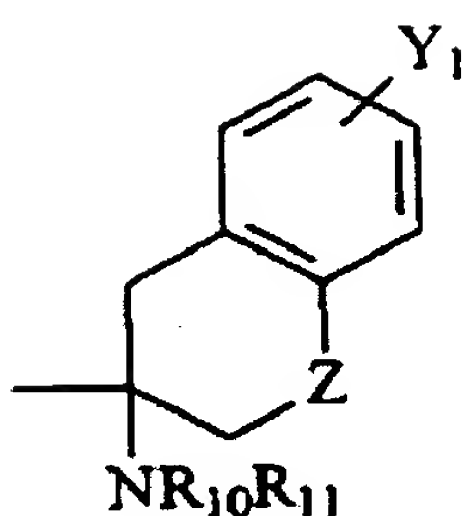


(i)

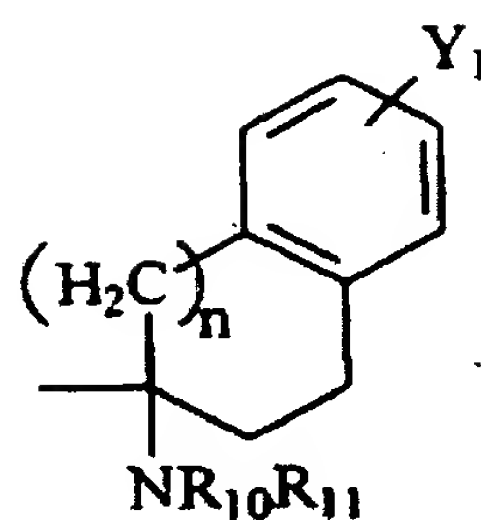




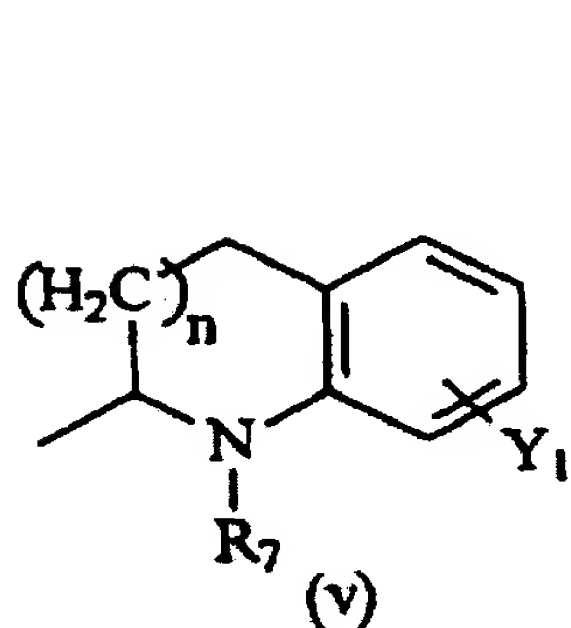
(s)



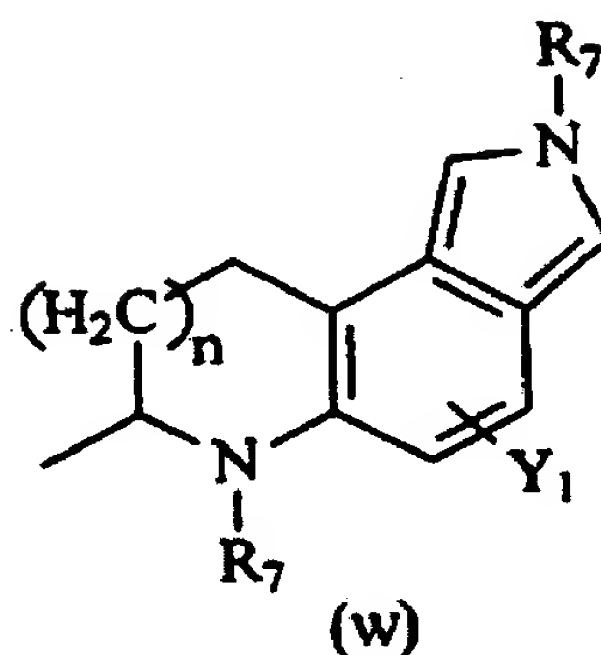
(t)



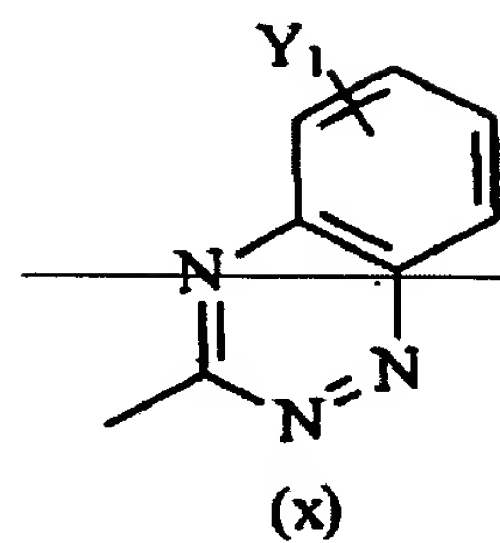
(u)



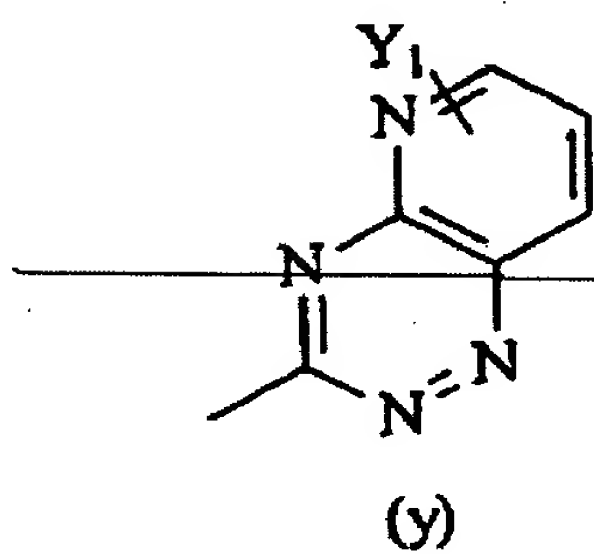
(v)



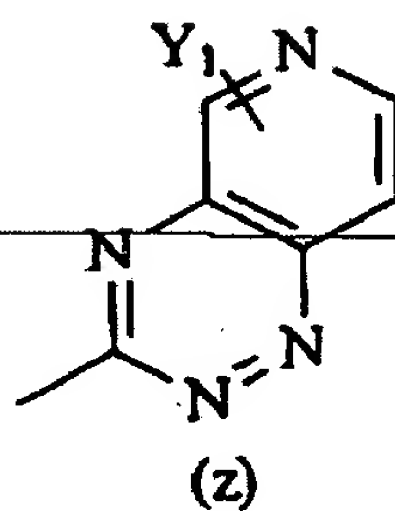
(w)



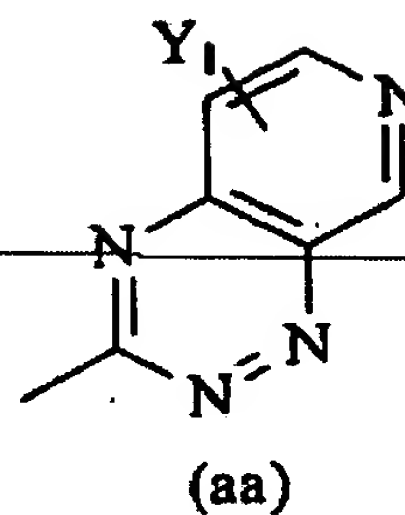
(x)



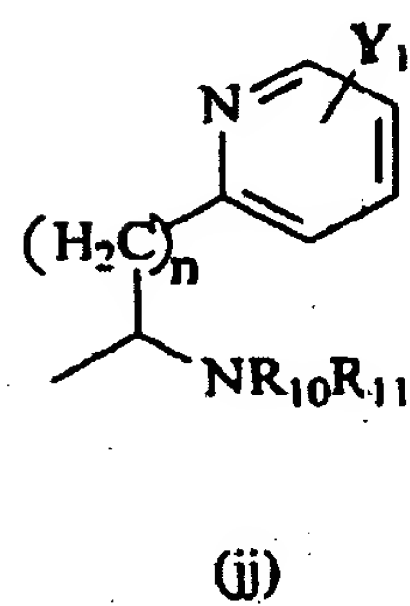
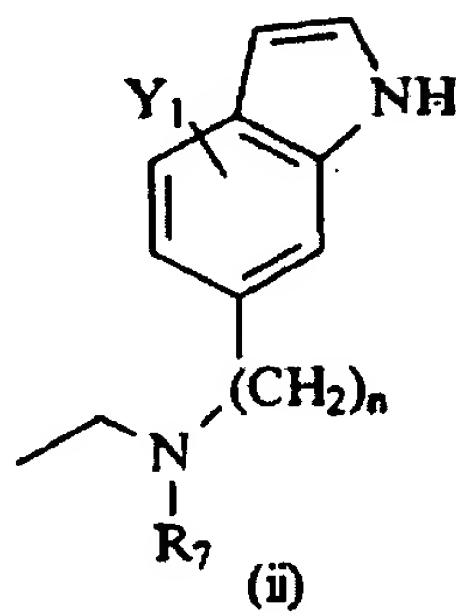
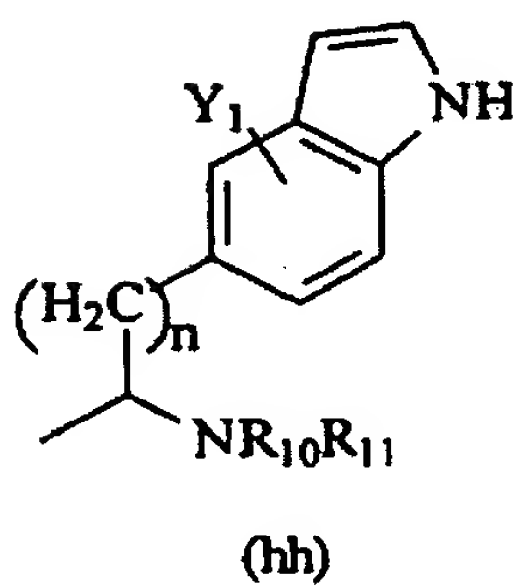
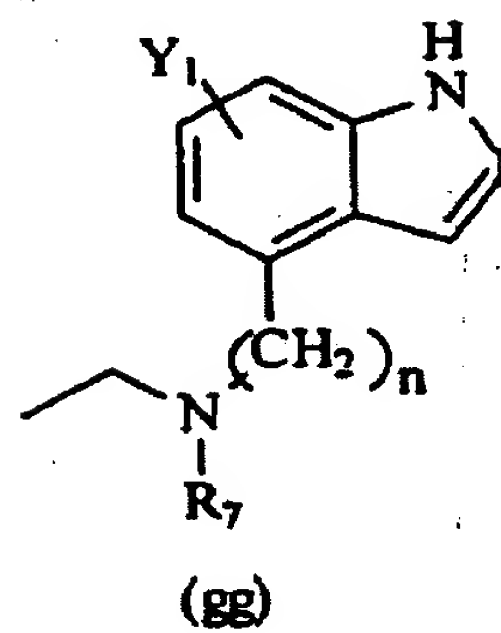
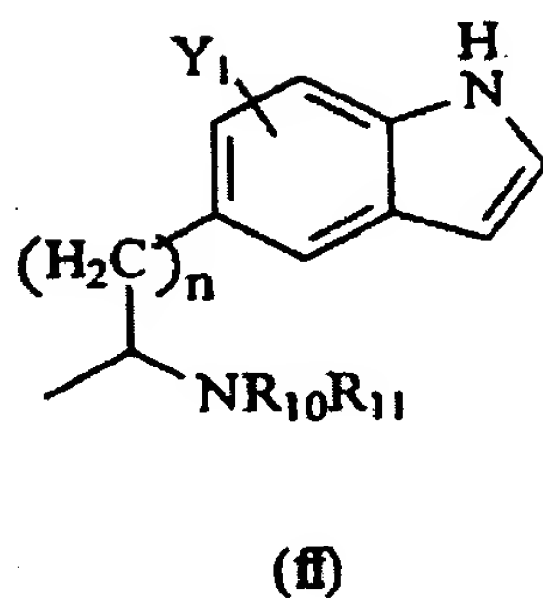
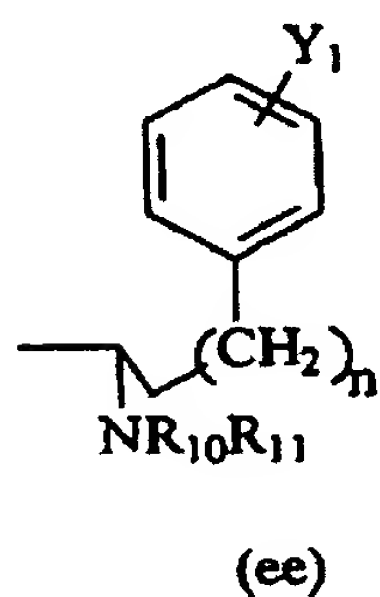
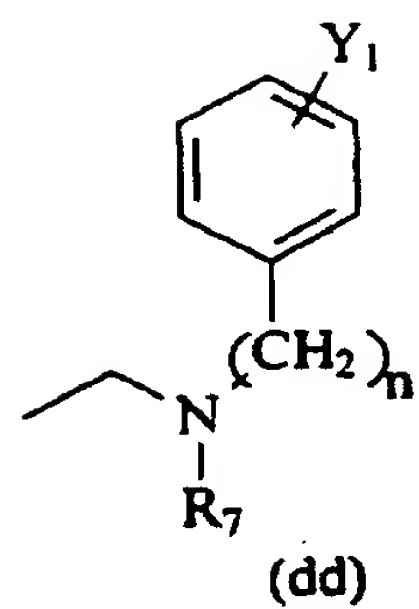
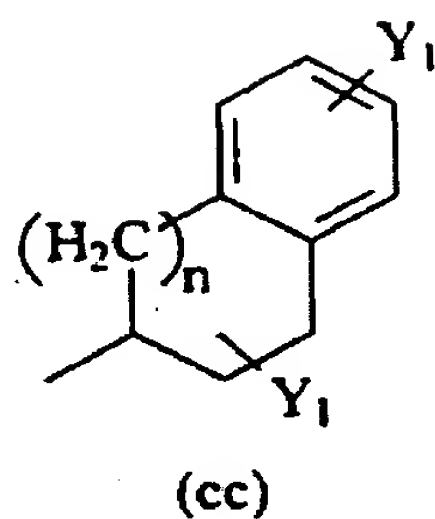
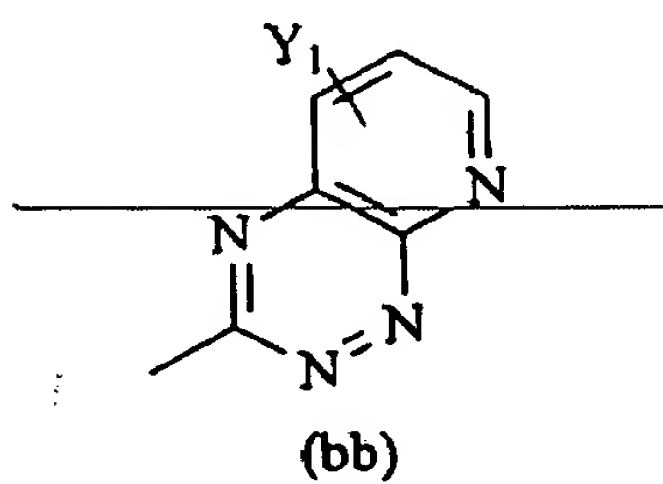
(y)

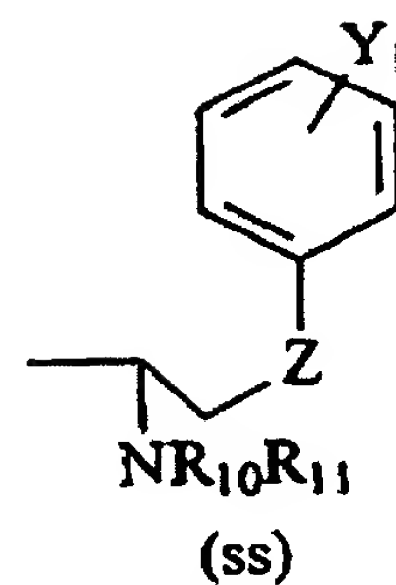
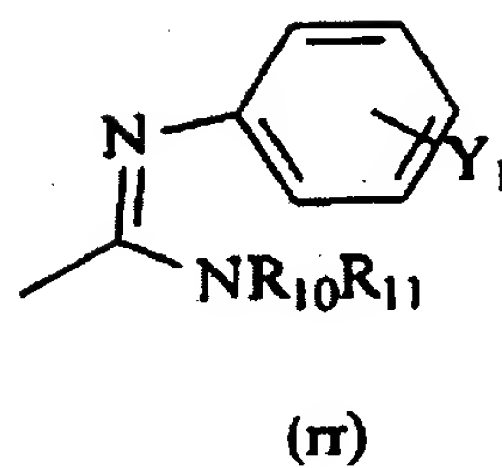
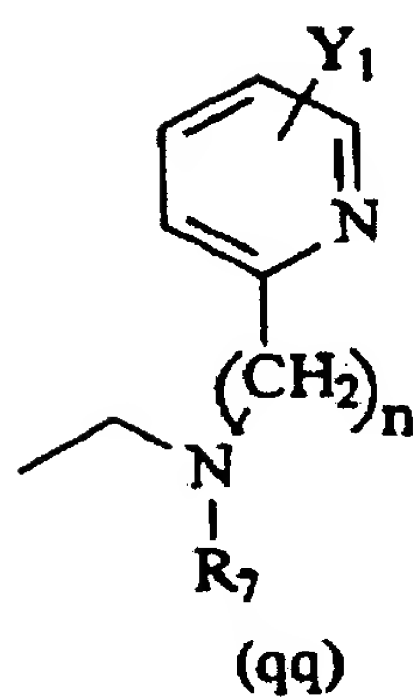
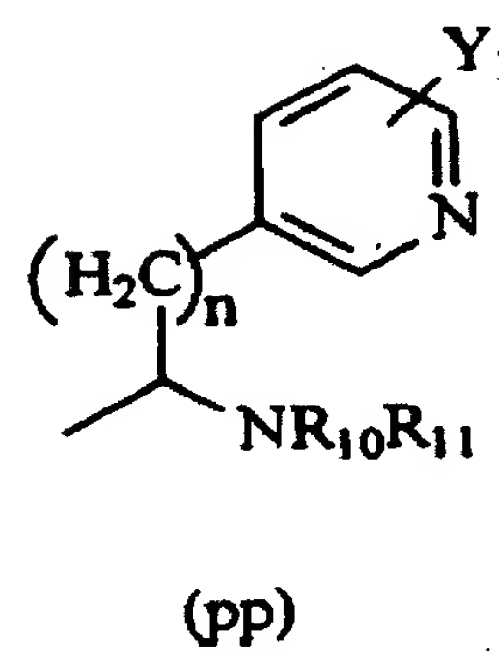
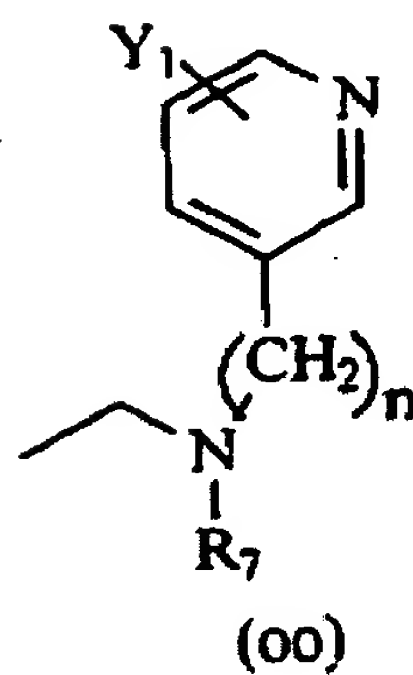
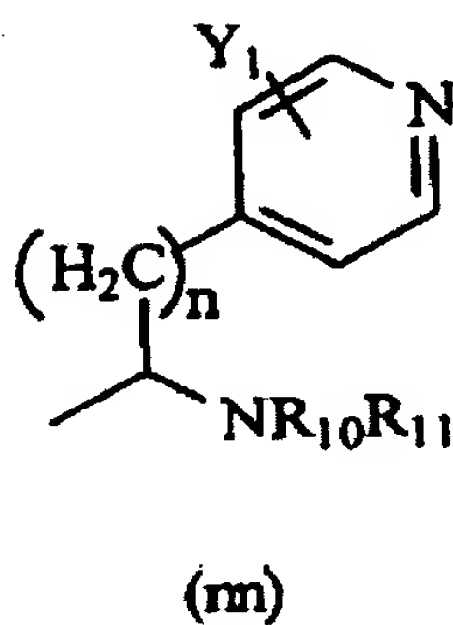
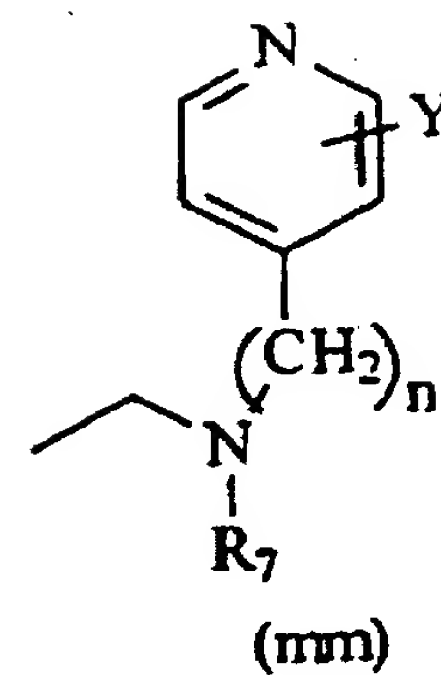
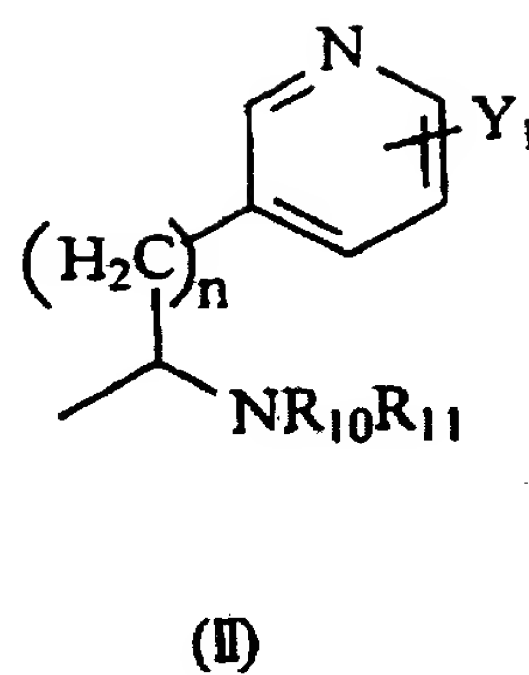
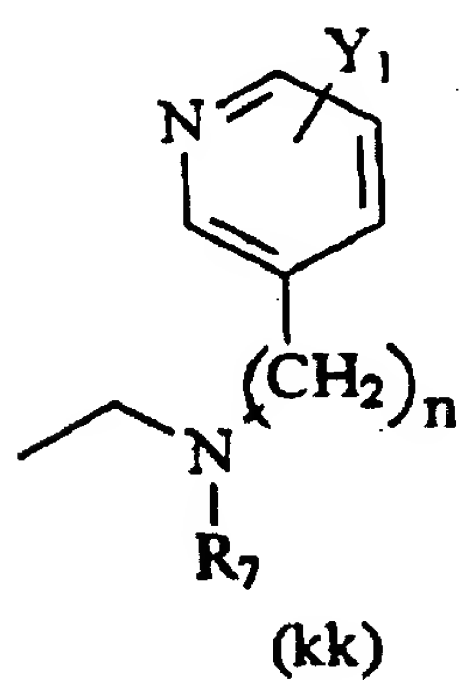


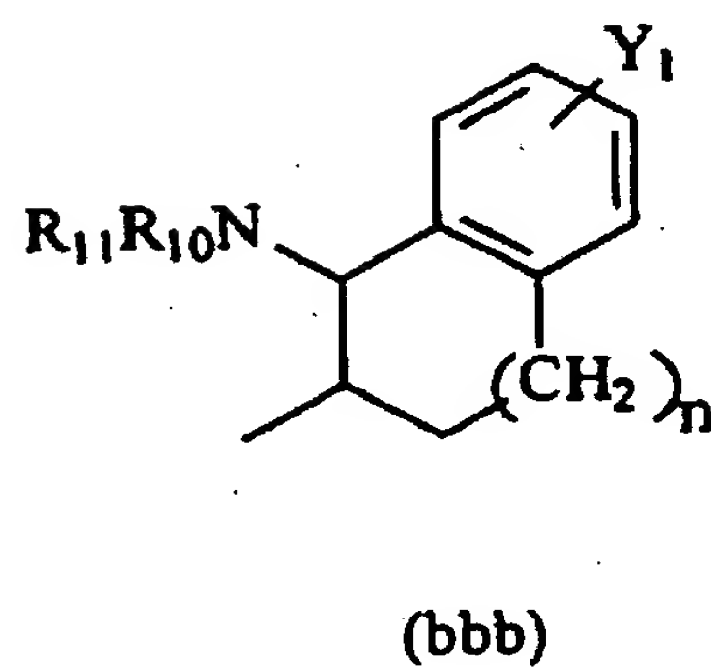
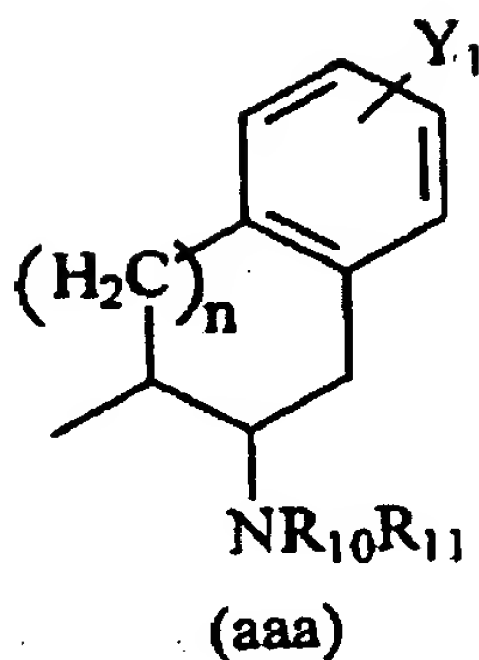
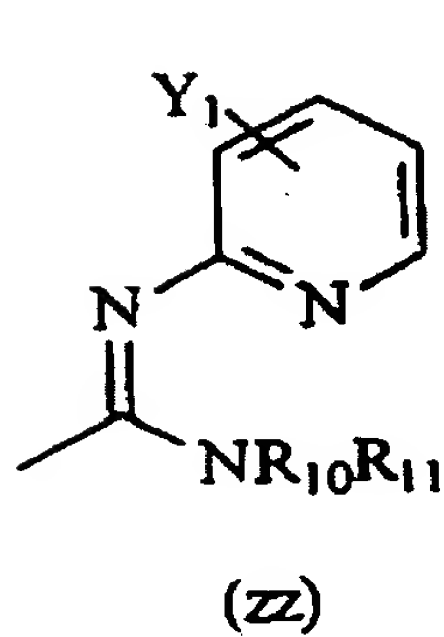
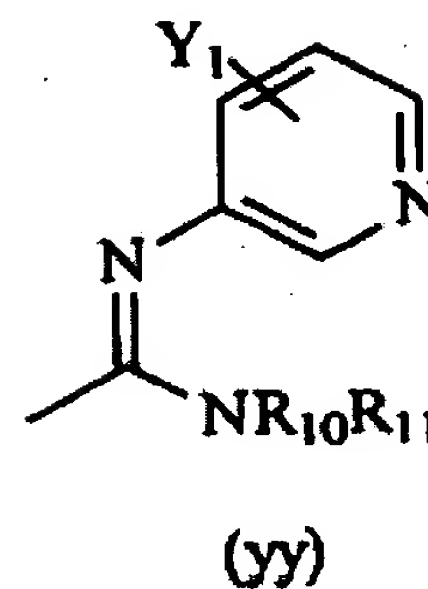
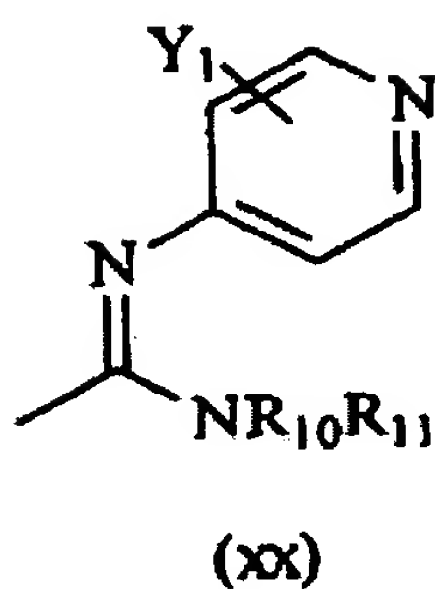
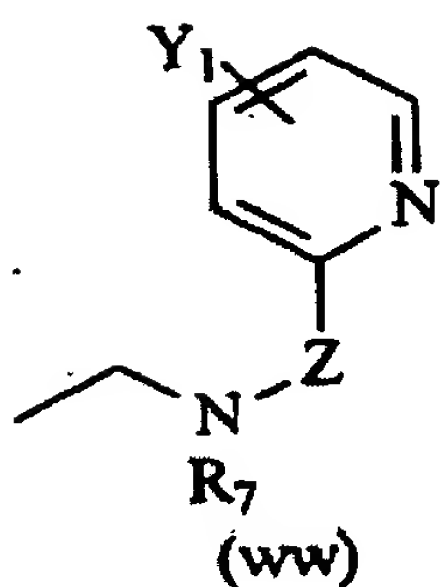
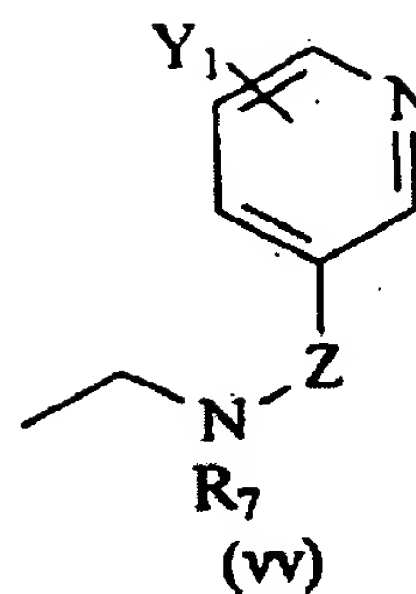
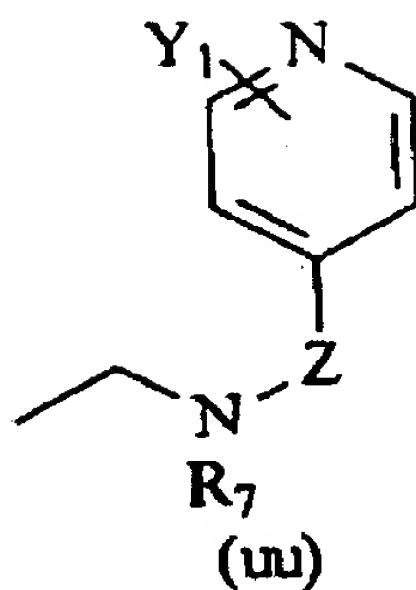
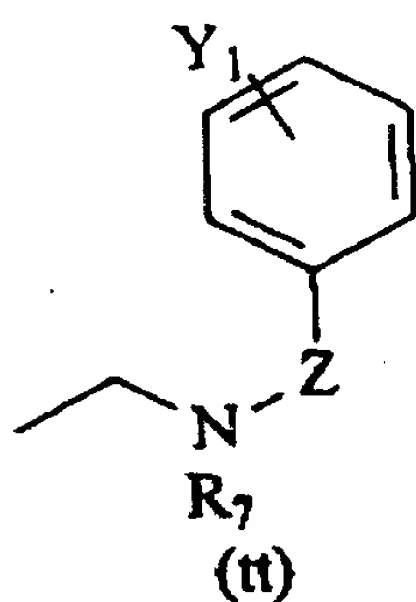
(z)



(aa)







X_1 is hydrogen, C_{1-8} alkyl, C_{3-8} alkenyl, or C_{3-8} alkynyl;

X_2 is hydrogen, C_{1-8} alkyl, C_{3-8} alkenyl, or C_{3-8} alkynyl; or

X_1 and X_2 together form $=O$, $=S$, $=NH$;

R_7 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , NR_{10} , R_{11} , $NHCOR_{12}$, $NHCO_2R_{13}$, $CONR_{14}R_{15}$, $CH_2(CH_2)_nY_2$, or $C(=NH)NR_{16}R_{17}$;

R_8 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents H, OH, Br, Cl, F, CN, CF_3 , NO_2 , N_3 , C_{1-6} alkyl, or $CH_2(CH_2)_nY_2'$; wherein Y_2' is H, CF_3 , or C_{1-6} alkyl;

R_9 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents H, OH, Br, Cl, F, CN, CF_3 , NO_2 , N_3 , C_{1-6} alkyl, or $CH_2(CH_2)_nY_2'$; wherein Y_2' is H, CF_3 , or C_{1-6} alkyl;

R_{10} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents H, OH, Br, Cl, F, CN, CF_3 , NO_2 , N_3 , C_{1-6} alkyl, or $CH_2(CH_2)_nY_2'$; wherein Y_2' is H, CF_3 , or C_{1-6} alkyl;

R_{11} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents H, OH, Br, Cl, F, CN, CF_3 , NO_2 , N_3 , C_{1-6} alkyl, or $CH_2(CH_2)_nY_2'$; wherein Y_2' is H, CF_3 , or C_{1-6} alkyl;

R_{12} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents H, OH, Br, Cl, F, CN, CF_3 , NO_2 , N_3 , C_{1-6} alkyl, or $CH_2(CH_2)_nY_2'$; wherein Y_2' is H, CF_3 , or C_{1-6} alkyl;

R_{13} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents H, OH, Br, Cl, F, CN, CF_3 , NO_2 , N_3 , C_{1-6} alkyl, or $CH_2(CH_2)_nY_2'$; wherein Y_2' is H, CF_3 , or C_{1-6} alkyl;

R_{14} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents H, OH, Br, Cl, F, CN, CF_3 , NO_2 , N_3 , C_{1-6} alkyl, or $CH_2(CH_2)_nY_2'$; wherein Y_2' is H, CF_3 , or C_{1-6} alkyl;

R_{15} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents H, OH, Br, Cl, F, CN, CF_3 , NO_2 , N_3 , C_{1-6} alkyl, or $CH_2(CH_2)_nY_2'$; wherein Y_2' is H, CF_3 , or C_{1-6} alkyl;

R_{16} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents H, OH, Br, Cl, F, CN, CF_3 , NO_2 , N_3 , C_{1-6} alkyl, or $CH_2(CH_2)_nY_2'$; wherein Y_2' is H, CF_3 , or C_{1-6} alkyl; and

R_{17} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents H, OH, Br, Cl, F, CN, CF_3 , NO_2 , N_3 , C_{1-6} alkyl, or $CH_2(CH_2)_nY_2'$; wherein Y_2' is H, CF_3 , or C_{1-6} alkyl;

and pharmaceutically acceptable salts thereof.

Claim 2 (Currently Amended): The method of claim 1, wherein said kappa opioid receptor antagonist is a compound of formula (I), wherein R_1 , R_4 , R_5 , Y_1 , Y_2 , Z , n , X_1 , X_2 , and R_7 - R_{17} are as in Claim 1;

Y_3 is H;

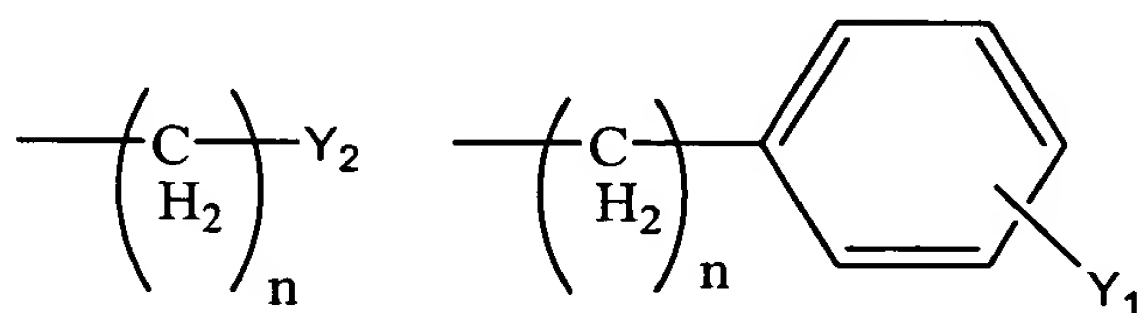
R_2 and R_3 are each, independently, H, C_{1-8} alkyl, C_{3-8} alkynyl, C_{3-8} alkynyl, or CH_2 aryl substituted by one or more substituents Y_1 ; and

R_6 is a group having a formula selected from the group consisting of structures (a)-(w) and (cc);

and pharmaceutically acceptable salts thereof.

3. (Previously Presented) The method of claim 1, wherein said kappa opioid receptor antagonist is a compound of formula (I) wherein Y_1 , Y_2 , R_4 , R_5 , Z , n , X_1 , X_2 and R_8 - R_{15} are as in Claim 1;

R_1 is C_{1-8} alkyl, or one of the following structures:



Y_3 is H;

R_2 and R_3 are each, independently, H or C_{1-8} alkyl, wherein R_2 and R_3 cannot both be H at the same time;

R_6 is a formula selected from the structures (a)-(r); and

R_7 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{13}$, $CONR_{14}R_{15}$, or $CH_2(CH_2)_nY_2$.

Claim 4 (Previously Presented) The method of claim 1, wherein said kappa opioid receptor antagonist is a compound of formula (I) wherein Y_1 , Z, n, X_1 , X_2 and R_8 - R_{15} are as in Claim 1;

R_1 is C_{1-8} alkyl;

Y_2 is H, CF_3 , CO_2R_9 , C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCO_2R_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, CH_2OH , CH_2OR_8 , or $COCH_2R_9$;

Y_3 is H;

R_2 and R_3 are each, independently, H or methyl, wherein R_2 and R_3 cannot both be H at the same time;

R_4 is H, C_{1-8} alkyl, CO_2C_{1-8} alkyl, or CH_2 aryl substituted by one or more substituents Y_1 and the stereocenter adjacent to R_4 is in an (S) configuration;

R_5 is H, C_{1-8} alkyl, or $CH_2CO_2C_{1-8}$ alkyl;

R_6 is a group having a formula selected from the group consisting of structures (a)-(c) and (h)-(o); and

R_7 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , $NR_{10}R_{11}$, $NHCO_2R_{12}$, $NHCO_2R_{13}$, $CONR_{14}R_{15}$, or $CH_2(CH_2)_nY_2$.

Claim 5 (Previously Presented) The method of claim 1, wherein said kappa opioid receptor antagonist is a compound of formula (I), wherein Y_1 , Z, n, X_1 , X_2 and R_8 - R_{14} are as in Claim 1;

R_1 is methyl,

Y_2 is H, CF_3 , CO_2R_9 , C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCO_2R_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, CH_2OH , CH_2OR_8 , or $COCH_2R_9$;

Y_3 is H;

R_2 and R_3 are each H or methyl, such that when R_2 is H, R_3 is methyl and vice versa;

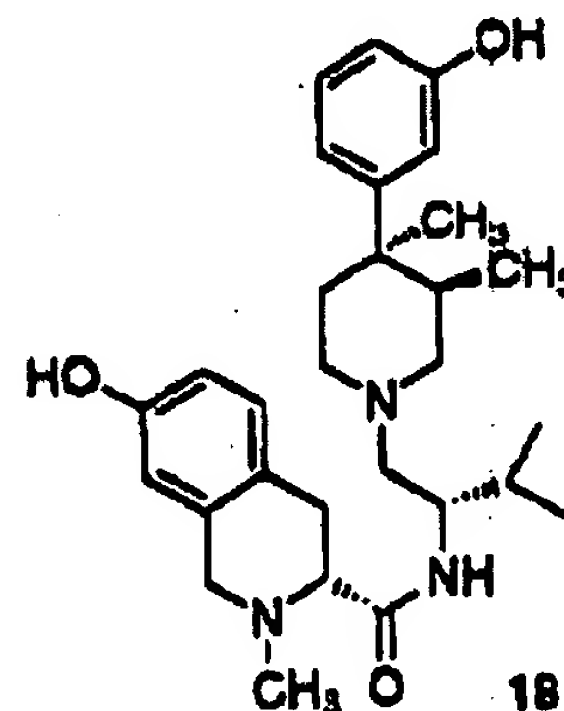
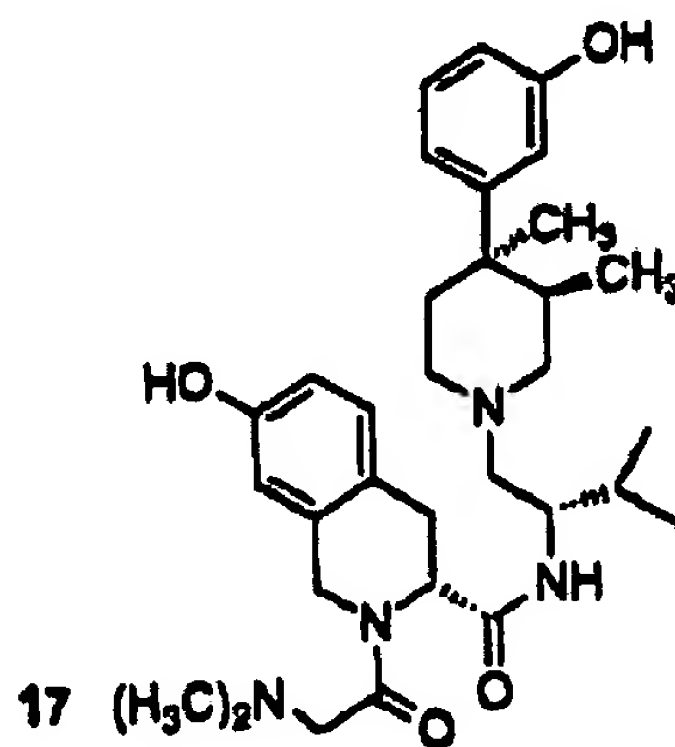
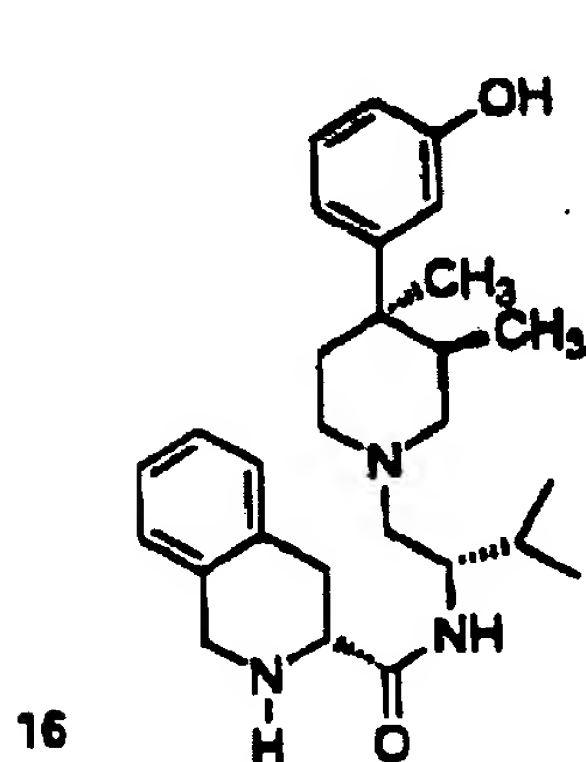
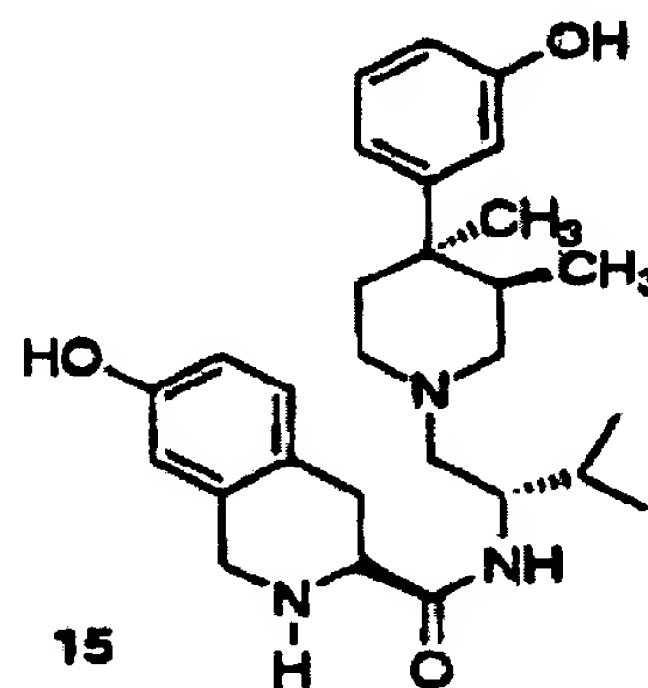
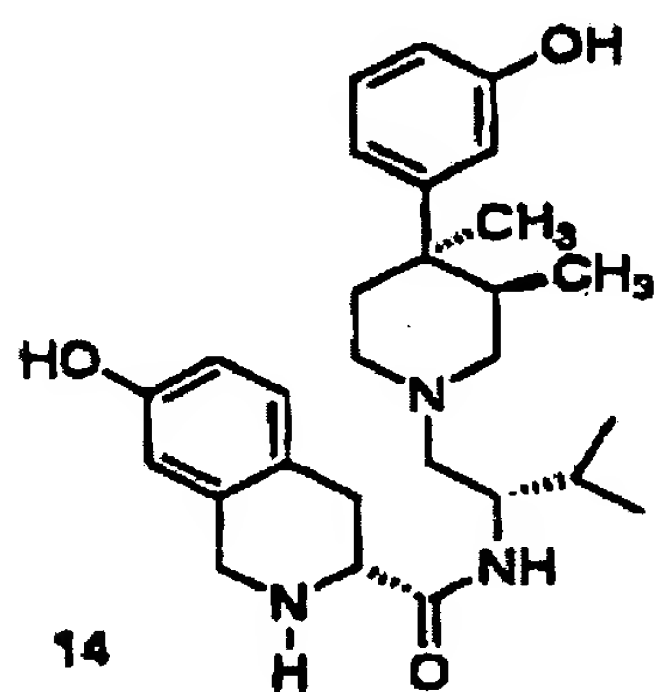
R_4 is C_{1-8} alkyl, or CO_2C_{1-8} alkyl, and the stereocenter adjacent to R_4 has a configuration of (S);

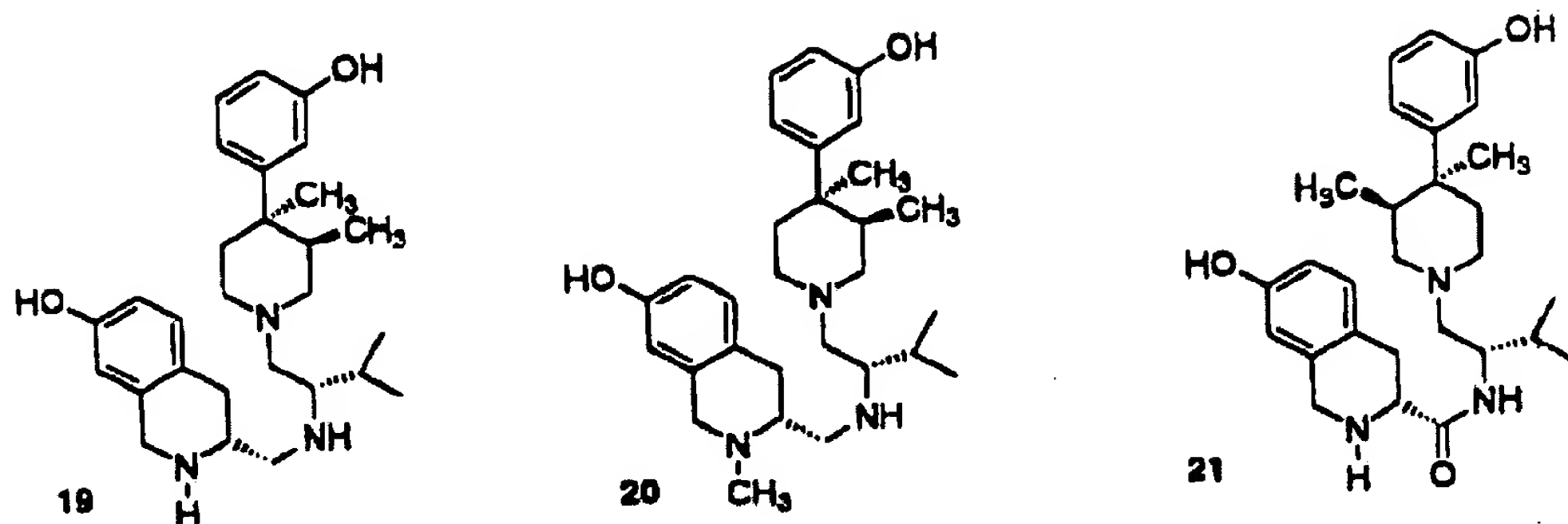
R_5 is H;

R_6 is a group having a formula selected from the group consisting of structures (a) and (b); and

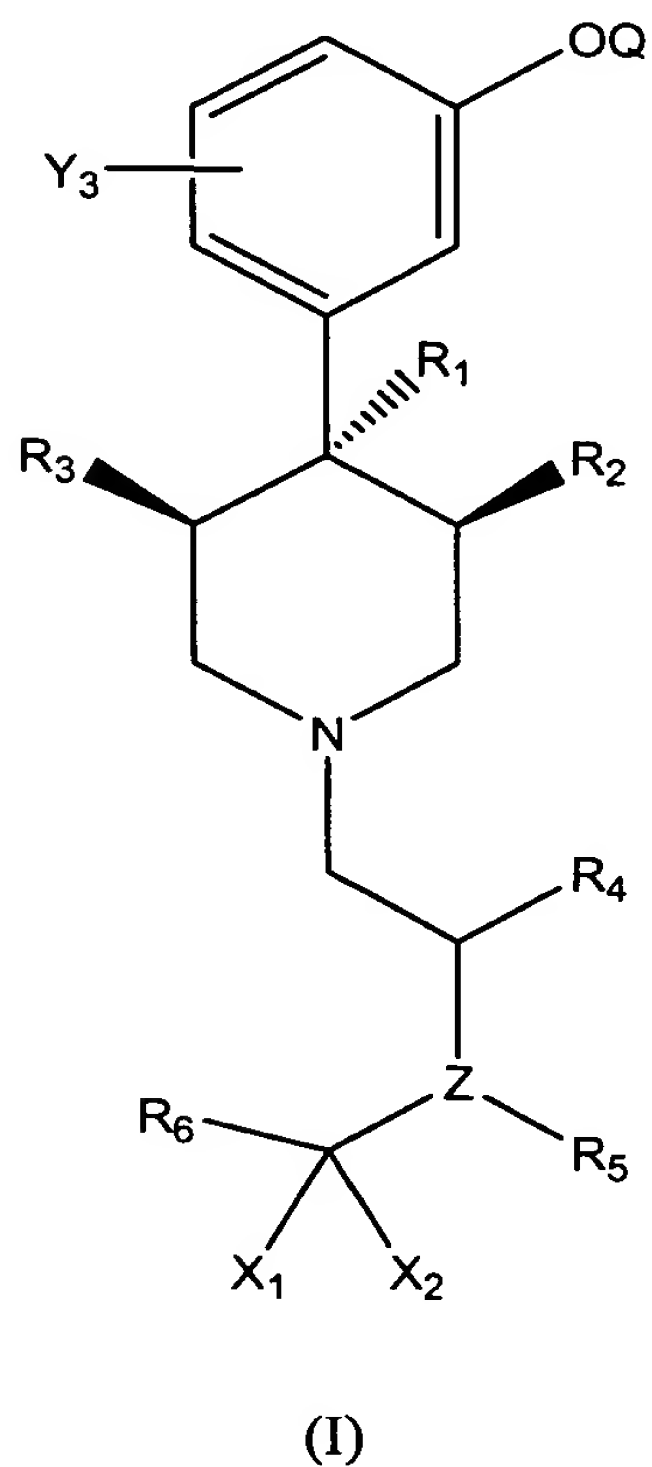
R_7 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$.

Claim 6 (Currently Amended) The method of claim 1, wherein said kappa opioid receptor antagonist is a compound selected from formulae 14-21 of Fig. 1 as follows:



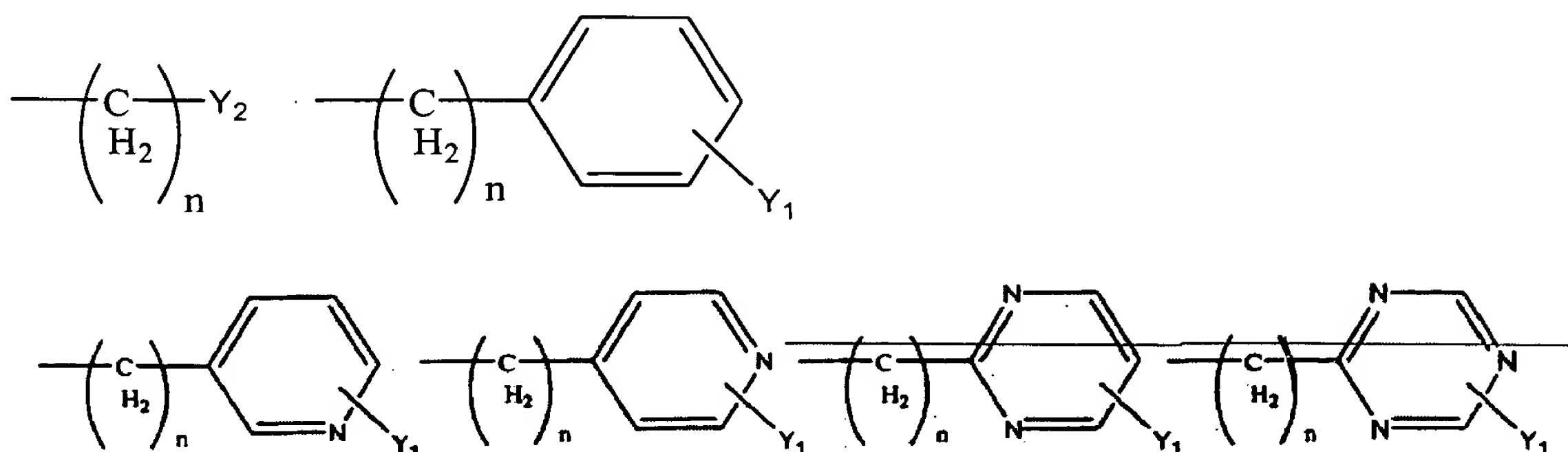


Claim 7 (Currently Amended) A kappa opioid receptor antagonist compound represented by the formula (I):



wherein Q is H or COC₁₋₈ alkyl;

R₁ is C₁₋₈ alkyl, or one of the following structures:



Y_1 is H, OH, Br, Cl, F, CN, CF_3 , NO_2 , N_3 , OR_8 , CO_2R_9 , C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, or $CH_2(CH_2)_n Y_2$;

Y_2 is H, CF_3 , CO_2R_9 , C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_3R_{14}$, CH_2OH , CH_2OR_8 , or $COCH_2R_9$;

Y_3 is H, OH, Br, Cl, F, CN, CF_3 , NO_2 , N_3 , OR_8 , CO_2R_9 , C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, or $CH_2(CH_2)_n Y_2$;

R_2 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl or CH_2 aryl substituted by one or more groups Y_1 ;

R_3 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl or CH_2 aryl substituted by one or more groups Y_1 ;

wherein R_2 and R_3 may be bonded together to form a C_{2-8} alkyl group;

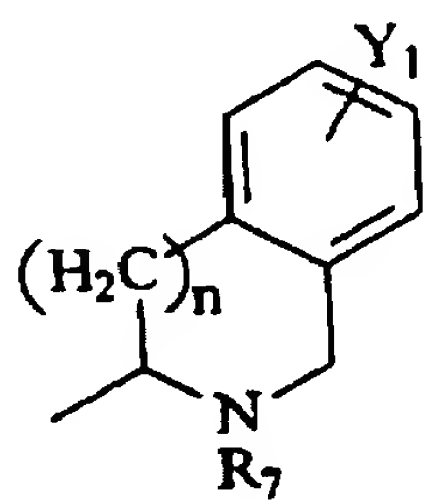
R_4 is hydrogen, C_{1-8} alkyl, CO_2C_{1-8} alkylaryl substituted by one or more groups Y_1 , CH_2 aryl substituted by one or more groups Y_1 or CO_2C_{1-8} alkyl;

Z is N, O or S; when Z is O or S there is no R_5

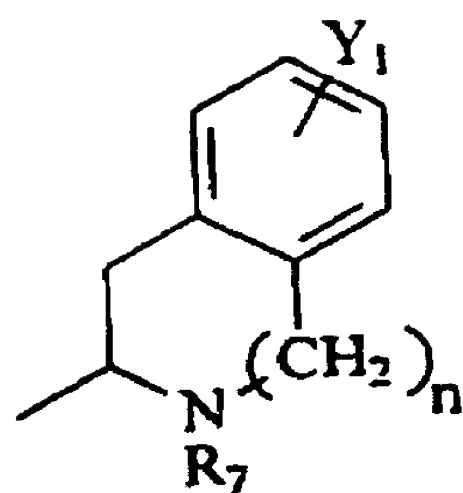
R_5 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, $CH_2CO_2C_{1-8}$ alkyl, CO_2C_{1-8} alkyl or CH_2 aryl substituted by one or more groups Y_1 ;

n is 0, 1, 2 or 3;

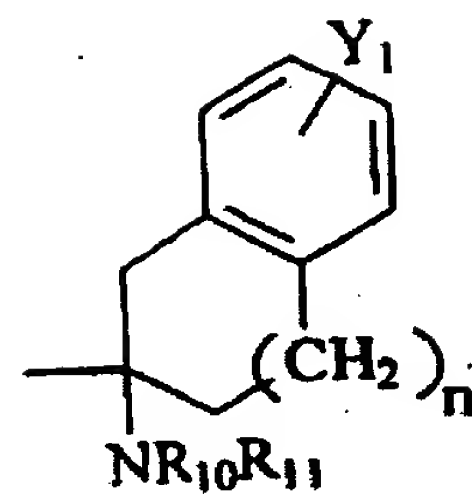
R_6 is a group selected from the group consisting of structures (a)-(w) and (cc)-(bbb):



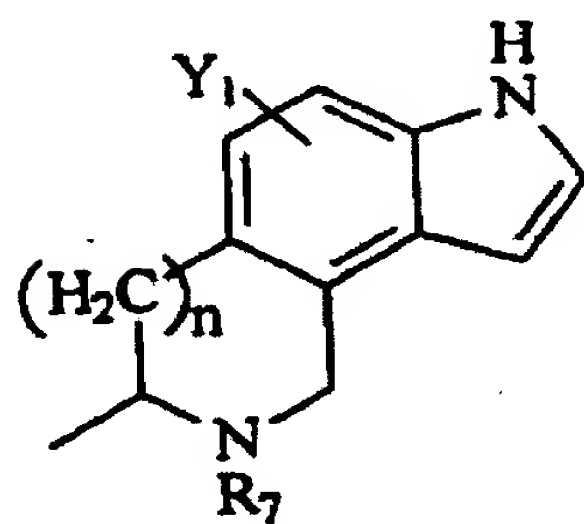
(a)



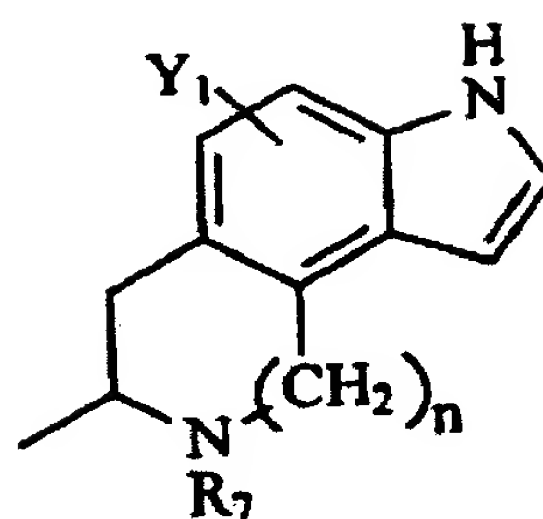
(b)



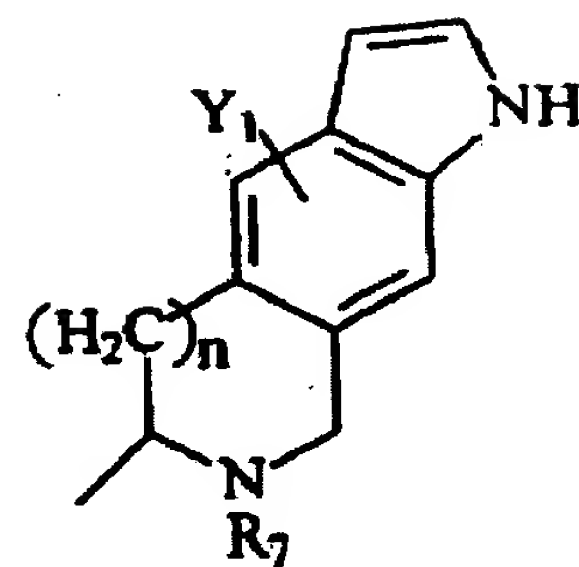
(c)



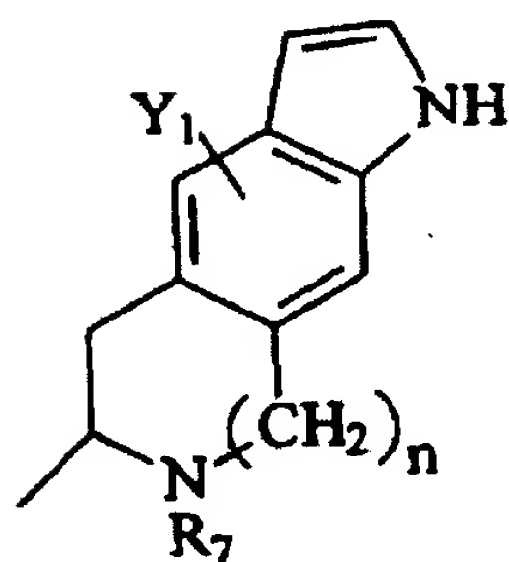
(d)



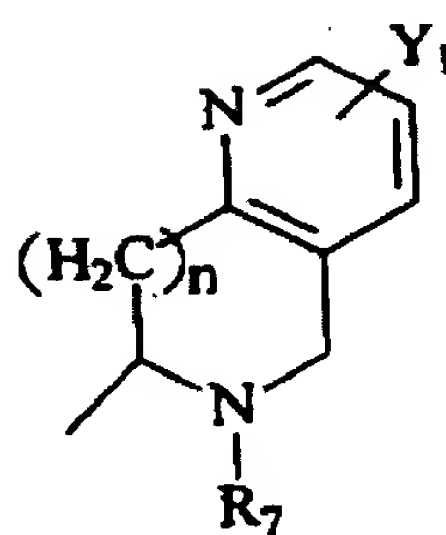
(e)



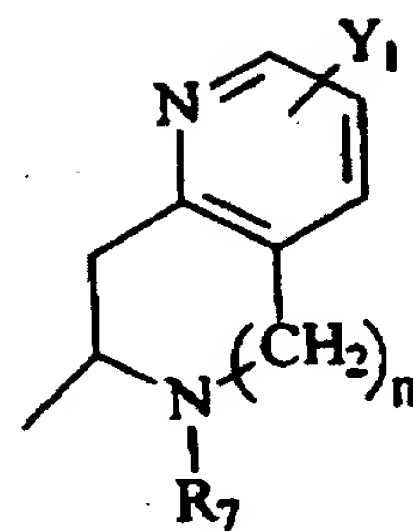
(f)



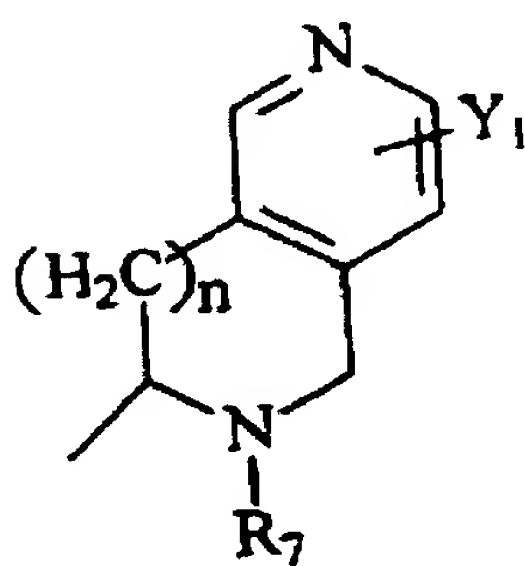
(g)



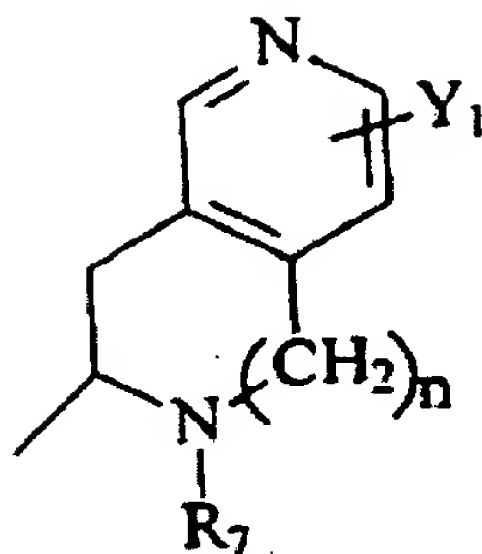
(h)



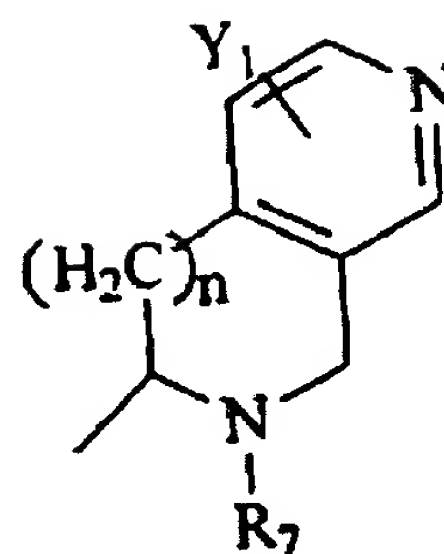
(i)



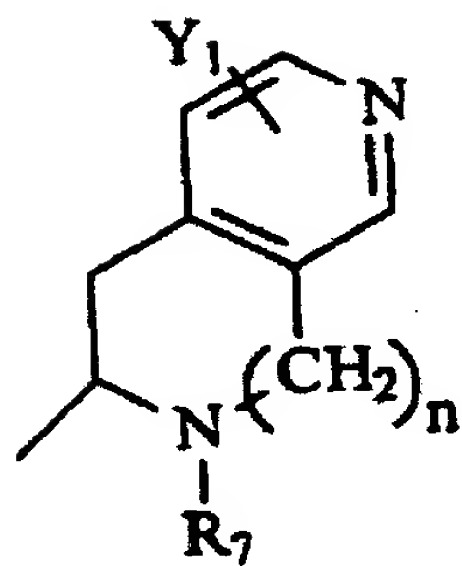
(j)



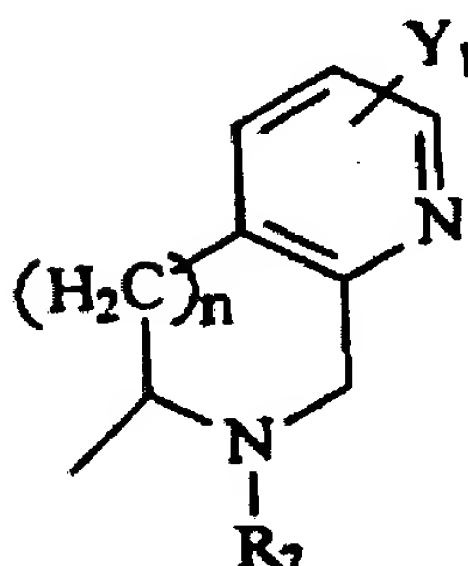
(k)



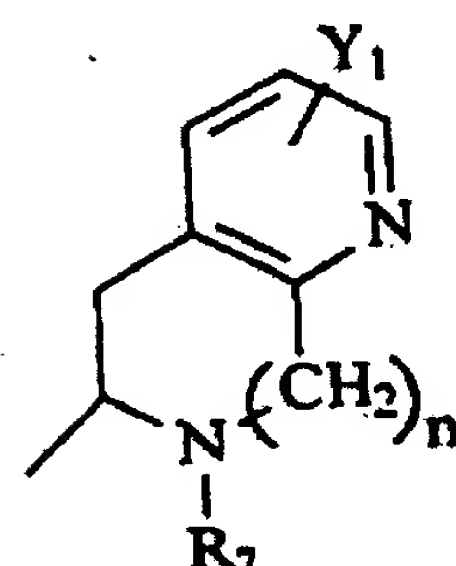
(l)



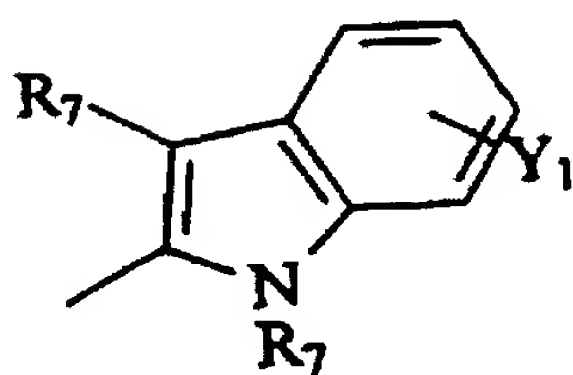
(m)



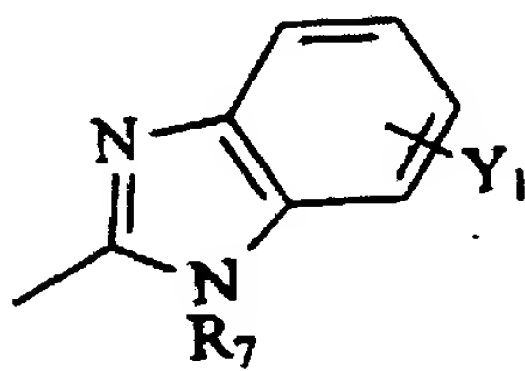
(n)



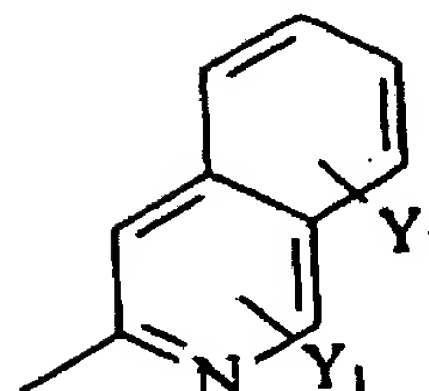
(o)



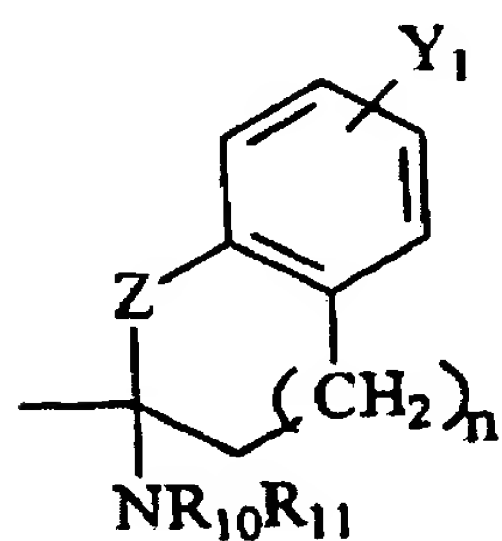
(p)



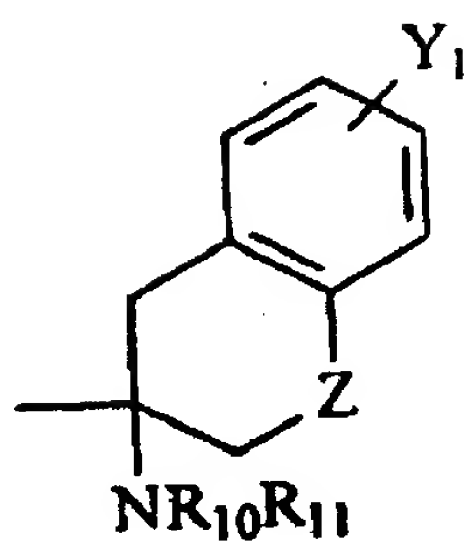
(q)



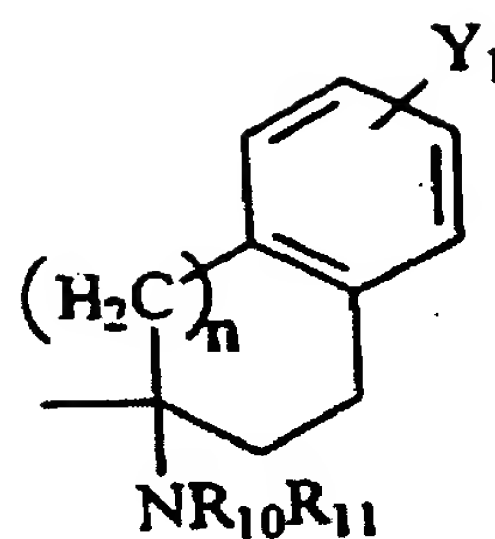
(r)



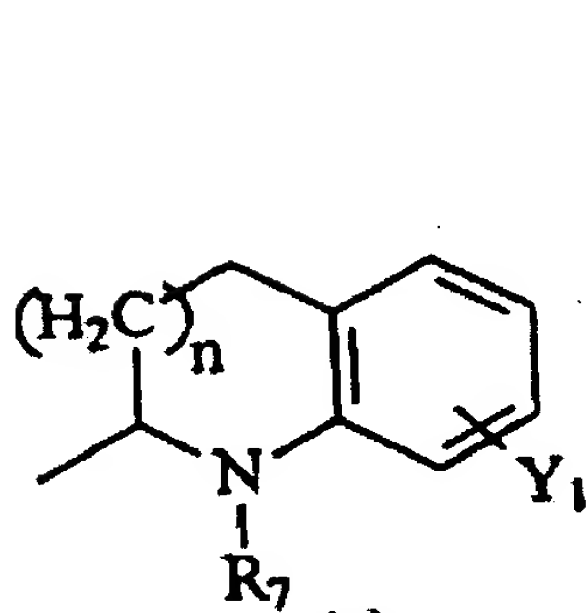
(s)



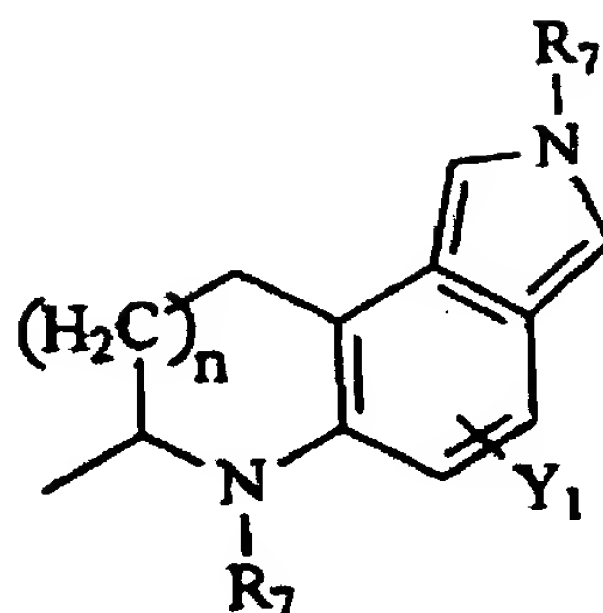
(t)



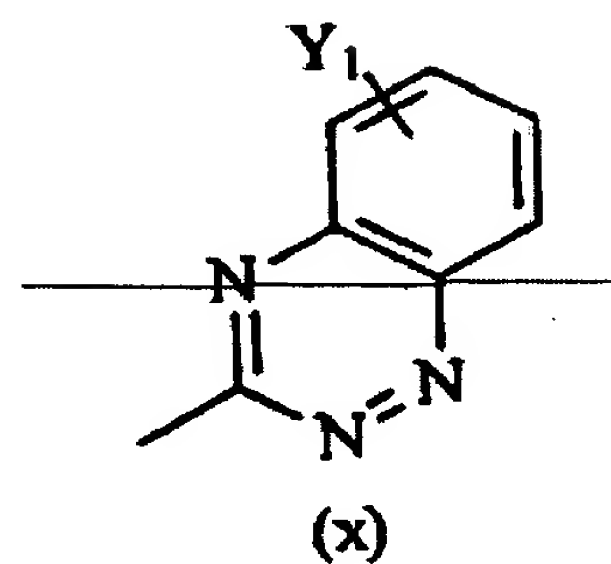
(u)



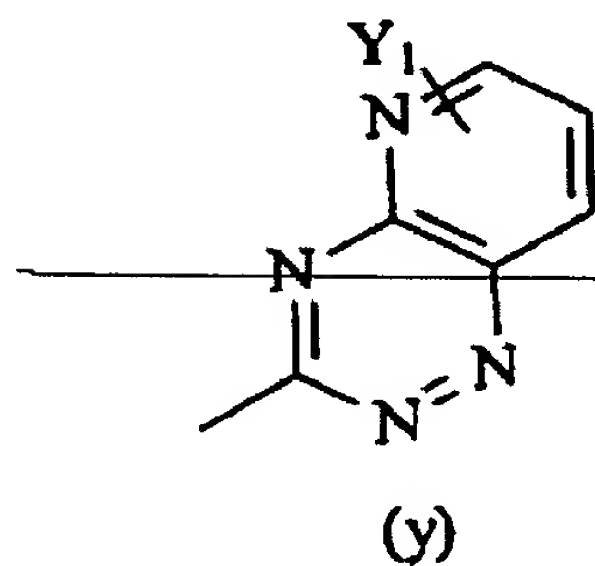
(v)



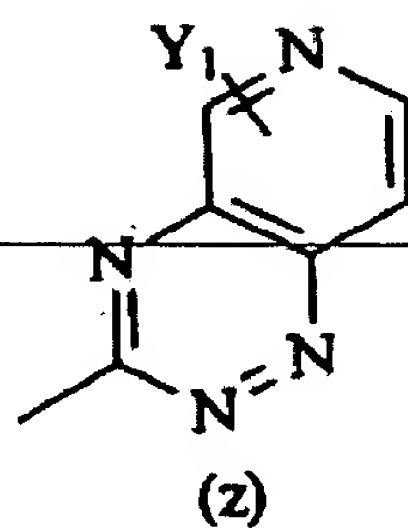
(w)



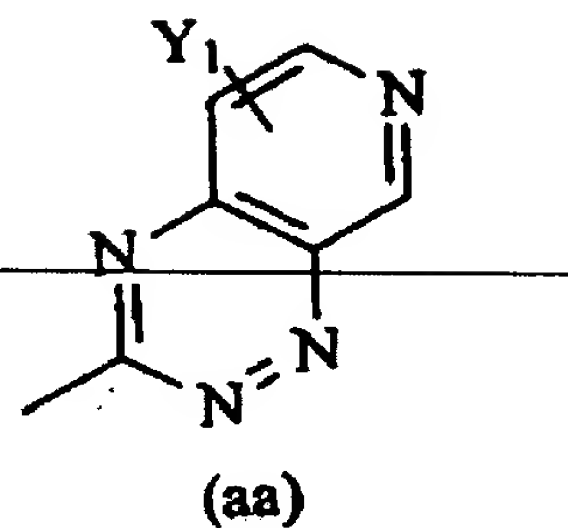
(x)



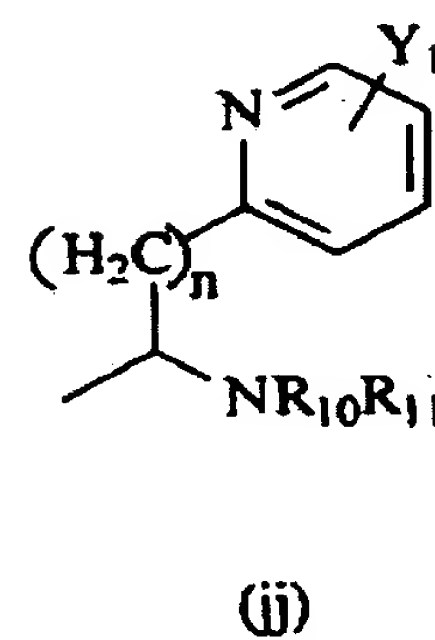
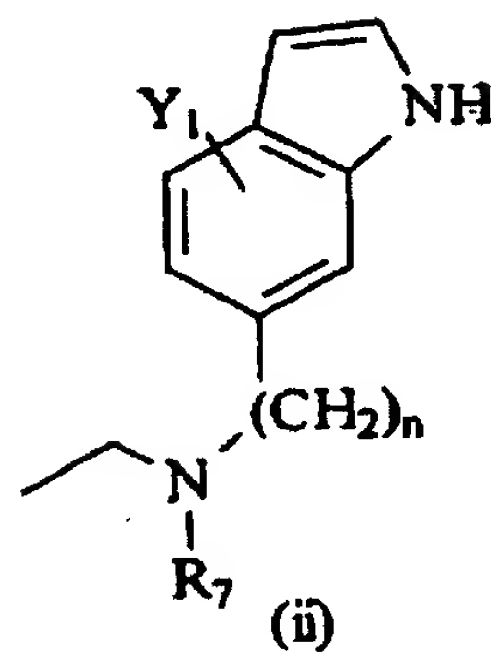
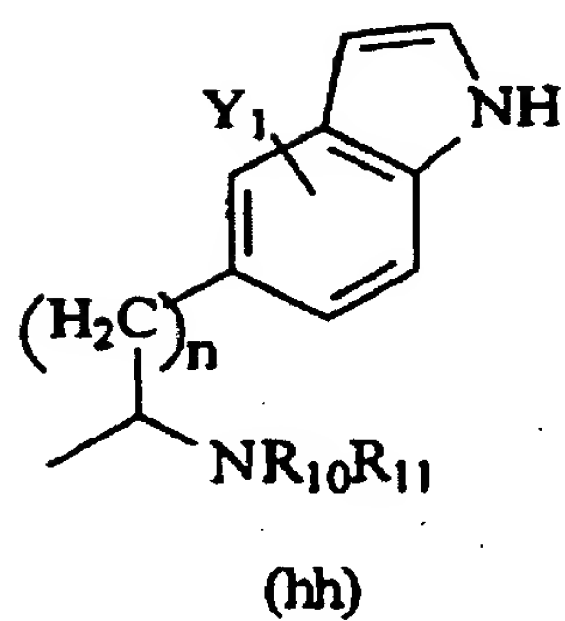
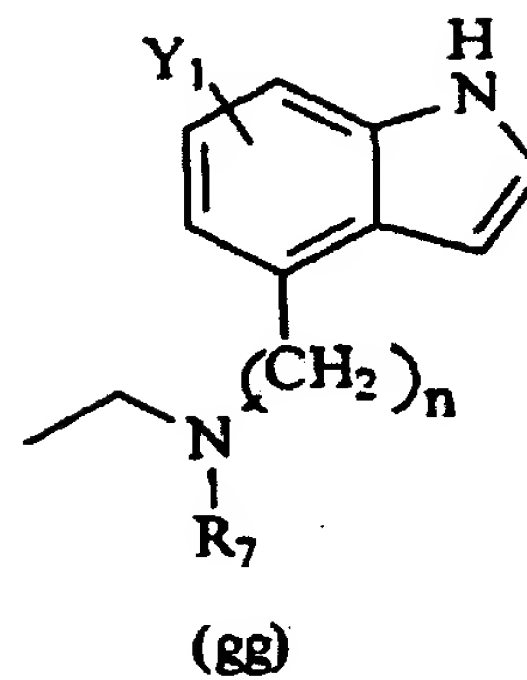
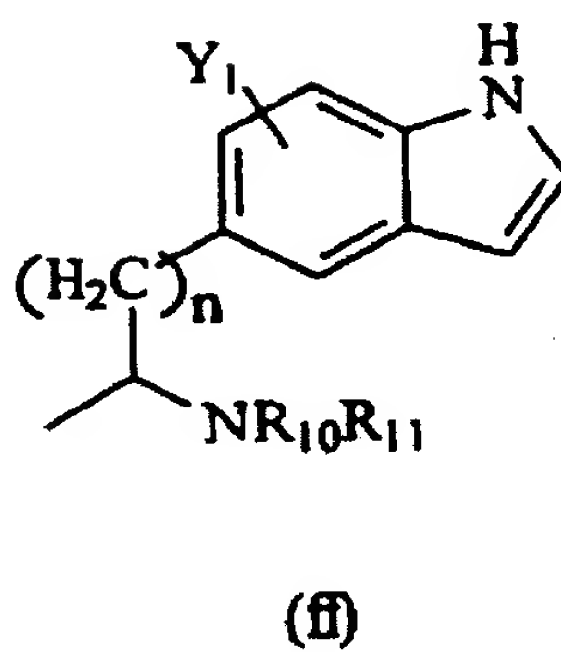
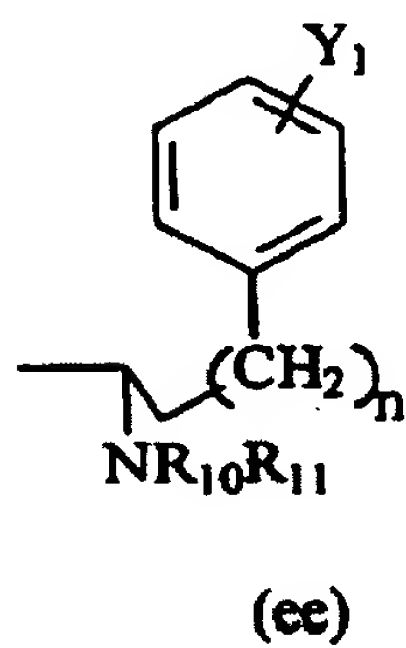
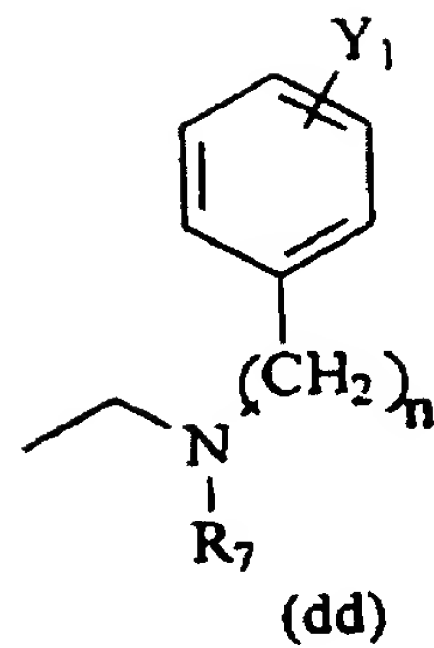
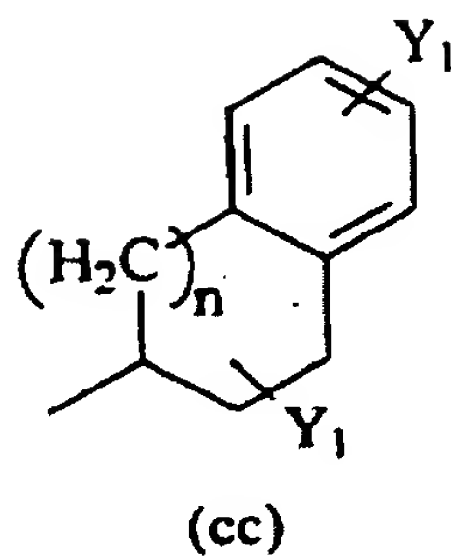
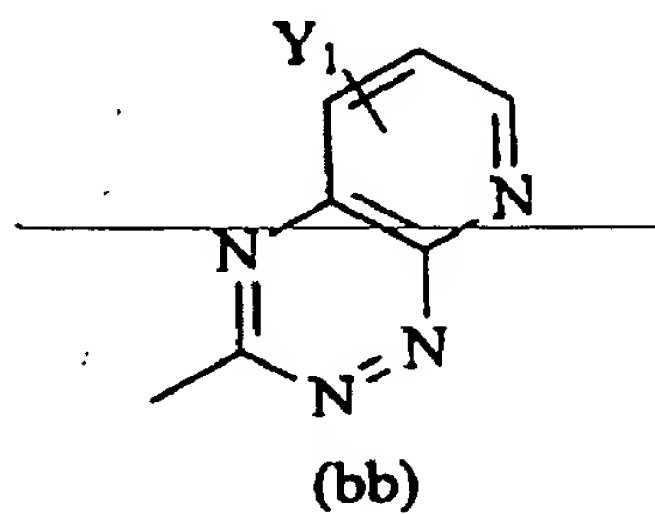
(y)

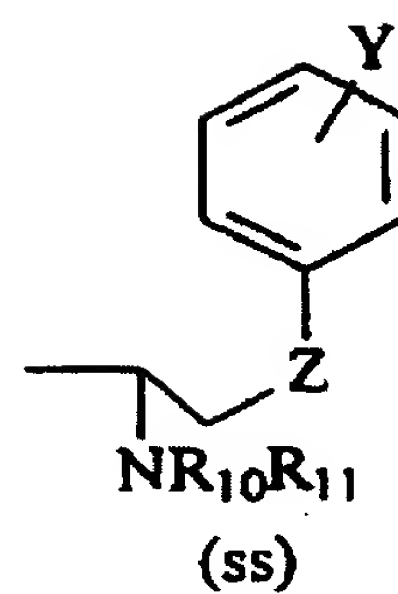
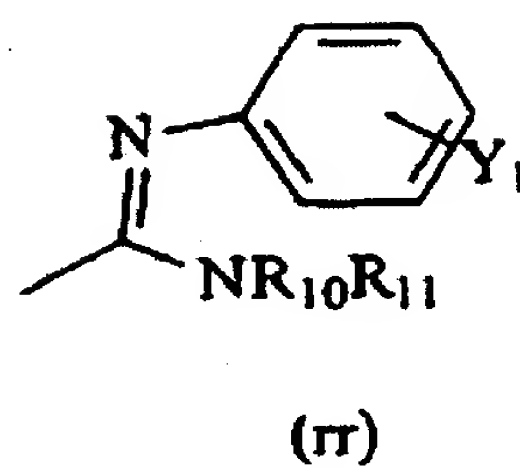
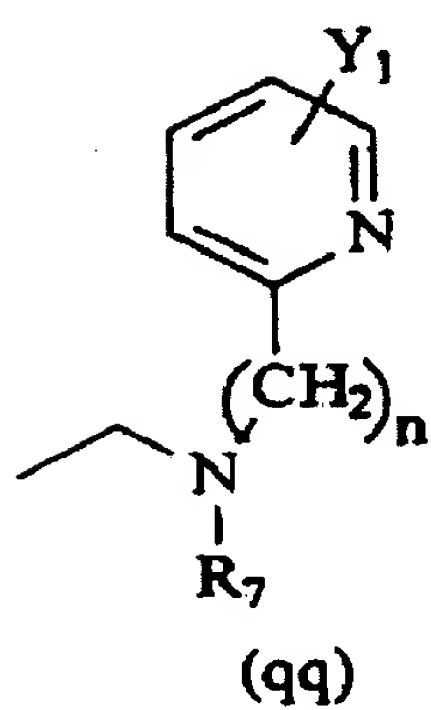
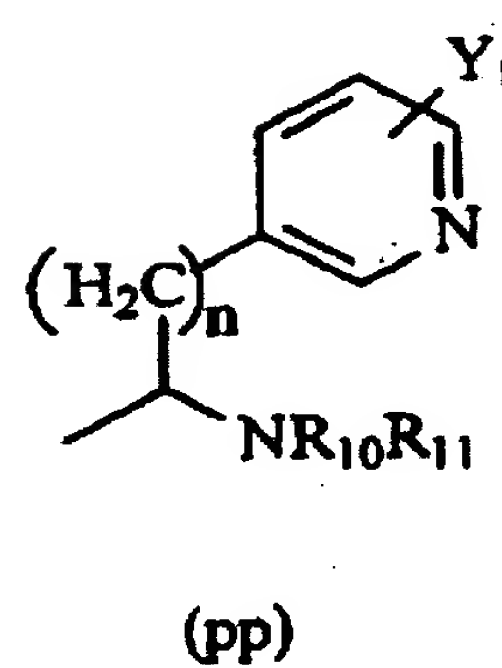
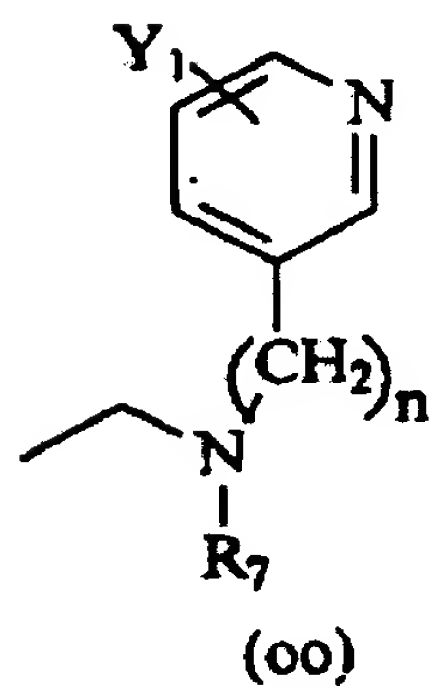
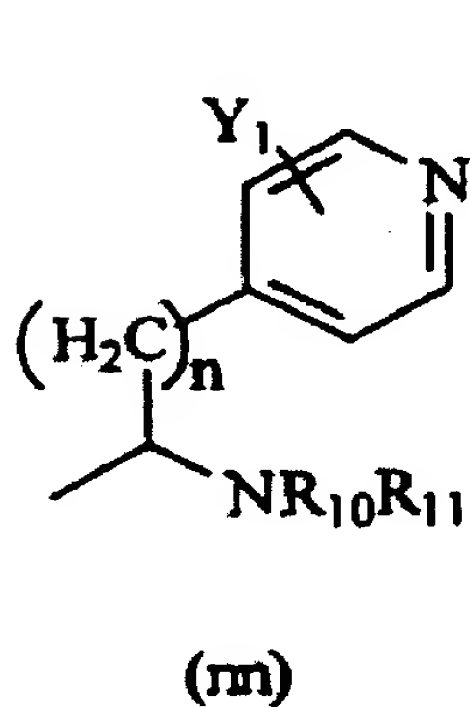
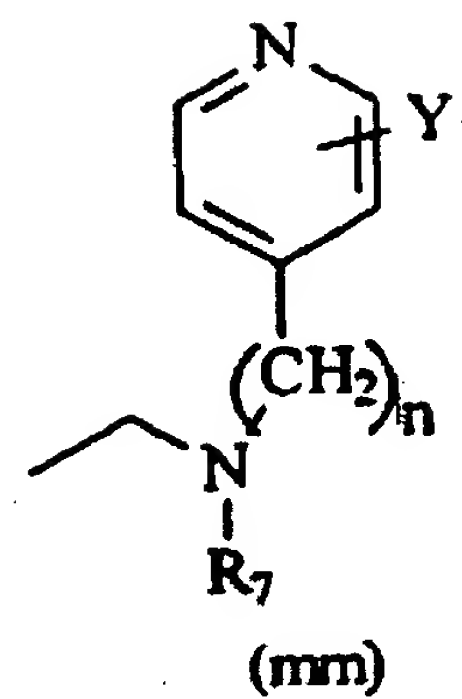
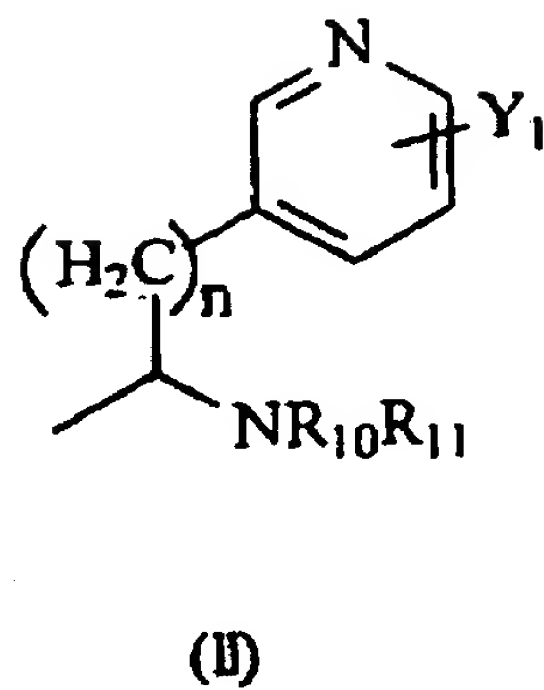
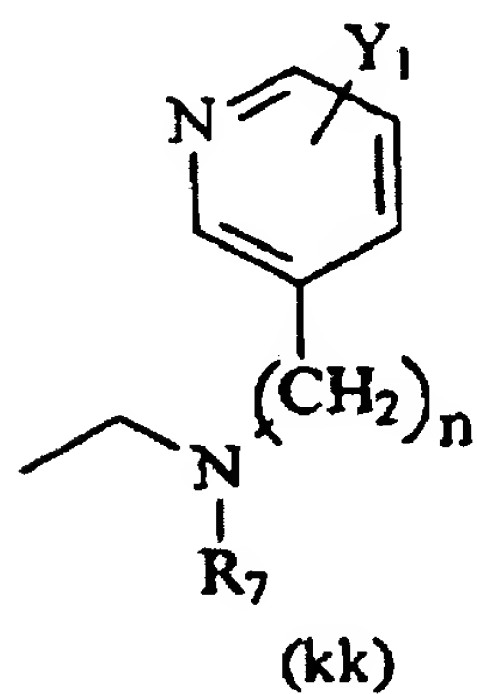


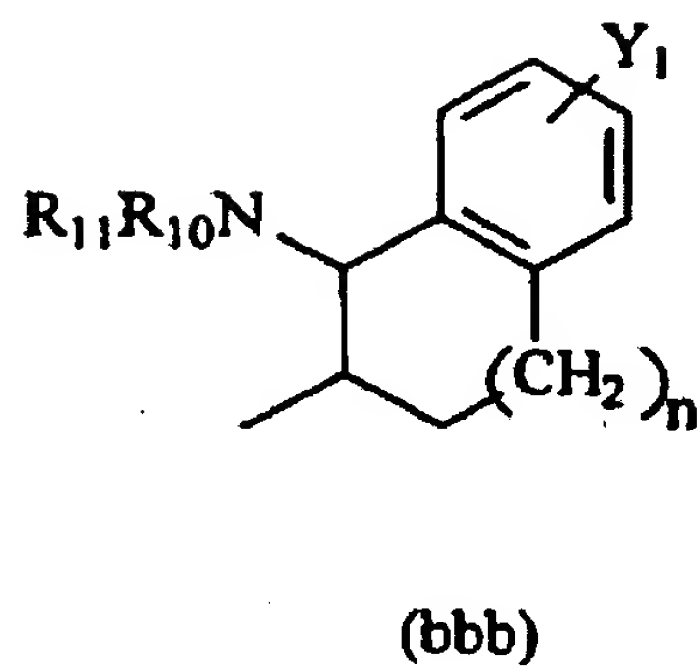
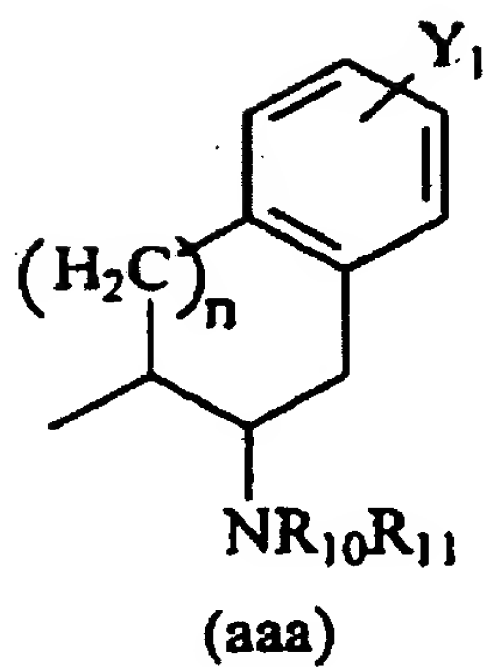
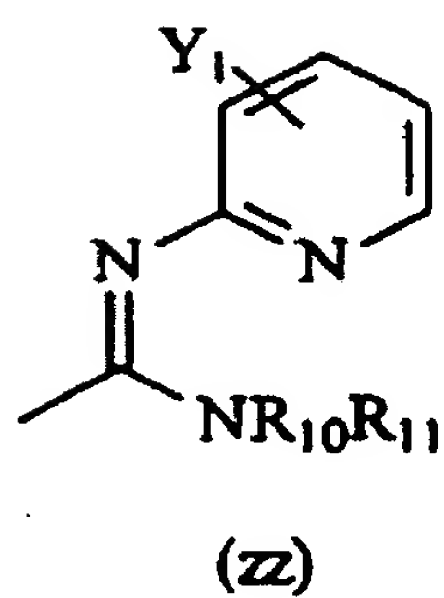
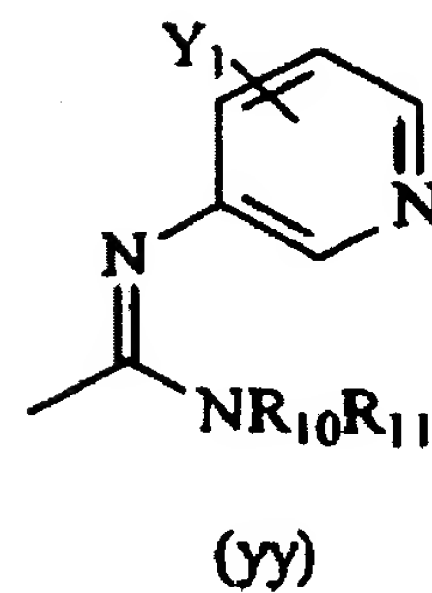
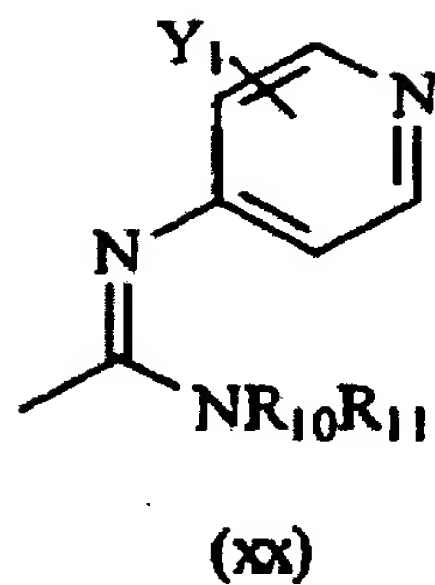
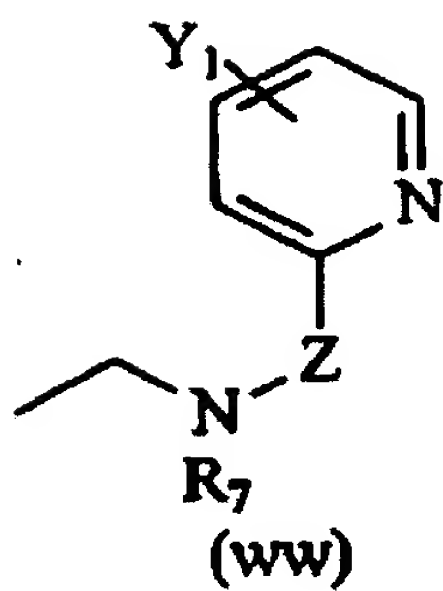
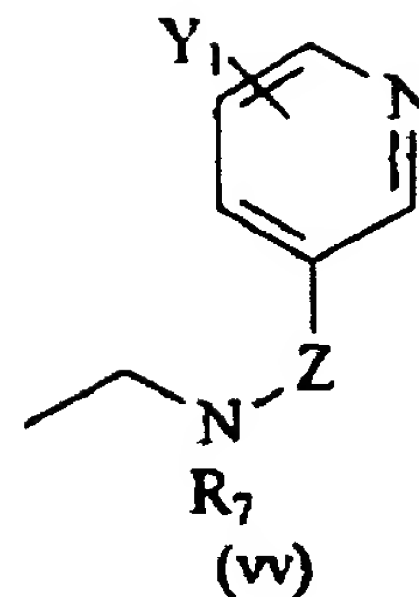
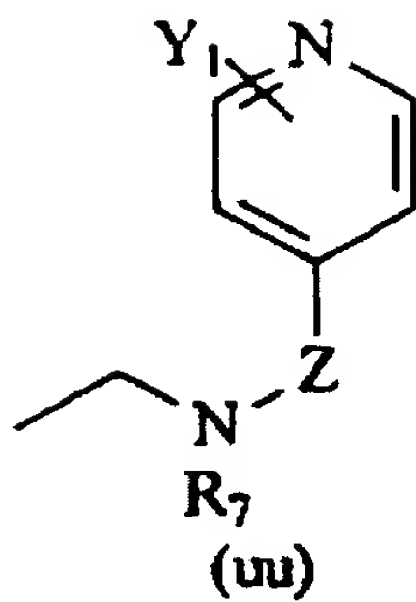
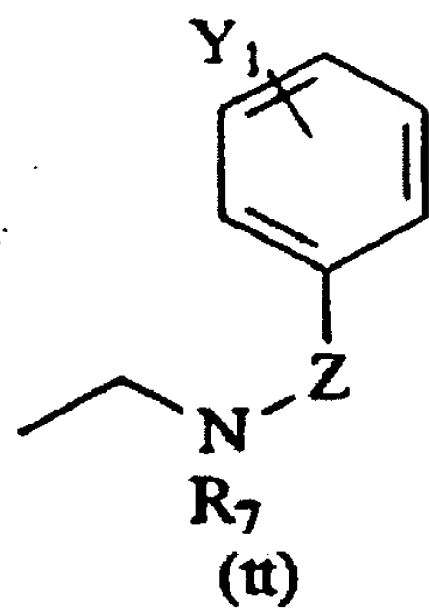
(z)



(aa)







X₁ is hydrogen, C₁₋₈ alkyl, C₃₋₈alkenyl, or C₃₋₈alkynyl;

X₂ is hydrogen, C₁₋₈alkyl, C₃₋₈alkenyl, or C₃₋₈alkynyl;

or X₁ and X₂ together form =O, =S, or =NH;

R₇ is H, C₁₋₈alkyl, CH₂aryl substituted by one or more substituents Y₁, NR₁₀R₁₁,
NHCOR₁₂, NHCO₂R₁₃, CONR₁₄R₁₅, CH₂(CH₂)_nY₂, or C(=NH)NR₁₆R₁₇;

R₈ is H, C₁₋₈alkyl, CH₂ aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆ alkyl, or CH₂(CH₂)_nY₂' ; wherein Y₂' is H, CF₃, or C₁₋₆alkyl;

R₉ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆ alkyl, or CH₂(CH₂)_nY₂' ; wherein Y₂' is H, CF₃, or C₁₋₆alkyl;

R₁₀ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆ alkyl, or CH₂(CH₂)_nY₂' ; wherein Y₂' is H, CF₃, or C₁₋₆alkyl ;

R₁₁ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆ alkyl, or CH₂(CH₂)_nY₂' ; wherein Y₂' is H, CF₃, or C₁₋₆alkyl ;

R₁₂ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆ alkyl, or CH₂(CH₂)_nY₂' ; wherein Y₂' is H, CF₃, or C₁₋₆alkyl ;

R₁₃ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆ alkyl, or CH₂(CH₂)_nY₂' ; wherein Y₂' is H, CF₃, or C₁₋₆alkyl ;

R₁₄ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆ alkyl, or CH₂(CH₂)_nY₂' ; wherein Y₂' is H, CF₃, or C₁₋₆alkyl ;

R₁₅ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆ alkyl, or CH₂(CH₂)_nY₂' ; wherein Y₂' is H, CF₃, or C₁₋₆alkyl ;

R₁₆ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆ alkyl, or CH₂(CH₂)_nY₂' ; wherein Y₂' is H, CF₃, or C₁₋₆alkyl ; and

R₁₇ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆ alkyl, or CH₂(CH₂)_nY₂' ; wherein Y₂' is H, CF₃, or C₁₋₆alkyl

and pharmaceutically acceptable salts thereof.

Claim 8 (Currently Amended) The kappa opioid receptor antagonist compound of claim 7, wherein R₁, R₄, R₅, Y₁, Y₂, Z, n, X₁, X₂, and R₇-R₁₇ are as in Claim 7;

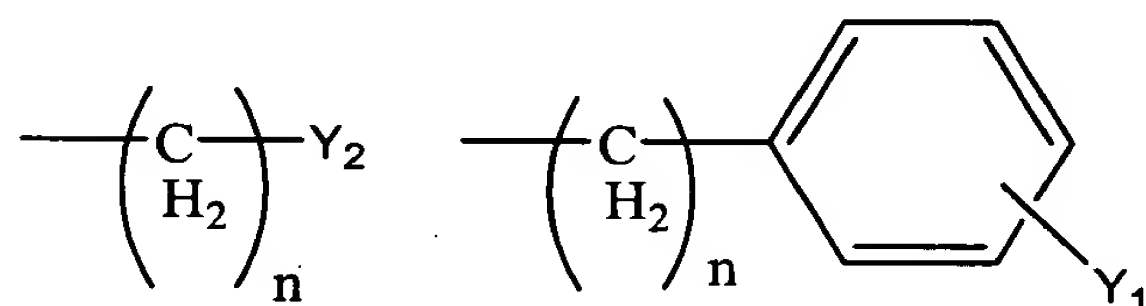
Y_3 is H;

R₂ and R₃ are each, independently, H, C₁₋₈ alkyl, C₃₋₈ alkynyl, C₃₋₈ alkynyl, or CH₂ary1 substituted by one or more substituents Y₁; and

R₆ is a group having a formula selected from the group consisting of structures (a)-(w) and (cc).

Claim 9 (Previously Presented) The kappa opioid receptor antagonist compound of claim 7, wherein Y₁, Y₂, R₄, R₅, Z, n, X₁, X₂ and R₈R₁₅ are as in Claim 7;

R₁ is C₁₋₈ alkyl, or one of the following structures:



Y_3 is H;

R₂ and R₃ are each, independently, H or C₁₋₈ alkyl, wherein R₂ and R₃ cannot both be H at the same time;

R₆ is a formula selected from the structures (a)-(r); and

R₇ is H, C₁₋₈ alkyl, CH₂ary₁ substituted by one or more substituents Y₁, NR₁₀R₁₁, NHCOR₁₂, NHCO₂R₁₃, CONR₁₄R₁₅, or CH₂(CH₂)_nY₂.

Claim 10 (Previously Presented) The kappa opioid receptor antagonist compound of claim 7, wherein Y₁, Z, n, X₁, X₂ and R₈-R₁₅ are as in Claim 7;

R_1 is C_{1-8} alkyl;

Y_2 is H, CF_3 , CO_2R_9 , C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$,
 CH_2OH , CH_2OR_8 , or $COCH_2R_9$;

Y_3 is H;

R_2 and R_3 are each, independently, H or methyl, wherein R_2 and R_3 cannot both be H
at the same time;

R_4 is H, C_{1-8} alkyl, CO_2C_{1-8} alkyl, or CH_2 aryl substituted by one or more substituents
 Y_1 and the stereocenter adjacent to R_4 is in an (S) configuration;

R_5 is H, C_{1-8} alkyl, $CH_2CO_2C_{1-8}$ alkyl;

R_6 is a group having a formula selected from the group consisting of structures (a)-(c)
and (h)-(o); and

R_7 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , $NR_{10}R_{11}$,
 $NHCOR_{12}$, $NHCO_2R_{13}$, $CONR_{14}R_{15}$, or $CH_2(CH_2)_nY_2$.

Claim 11 (Previously Presented) The kappa opioid receptor antagonist compound of
claim 7, wherein Y_1 , Z, n, X_1 , X_2 and R_8 - R_{14} are as in Claim 7;

R_1 is methyl,

Y_2 is H, CF_3 , CO_2R_9 , C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$,
 CH_2OH , CH_2OR_8 , or $COCH_2R_9$;

Y_3 is H;

R_2 and R_3 are each H or methyl, such that when R_2 is H, R_3 is methyl and vice versa;

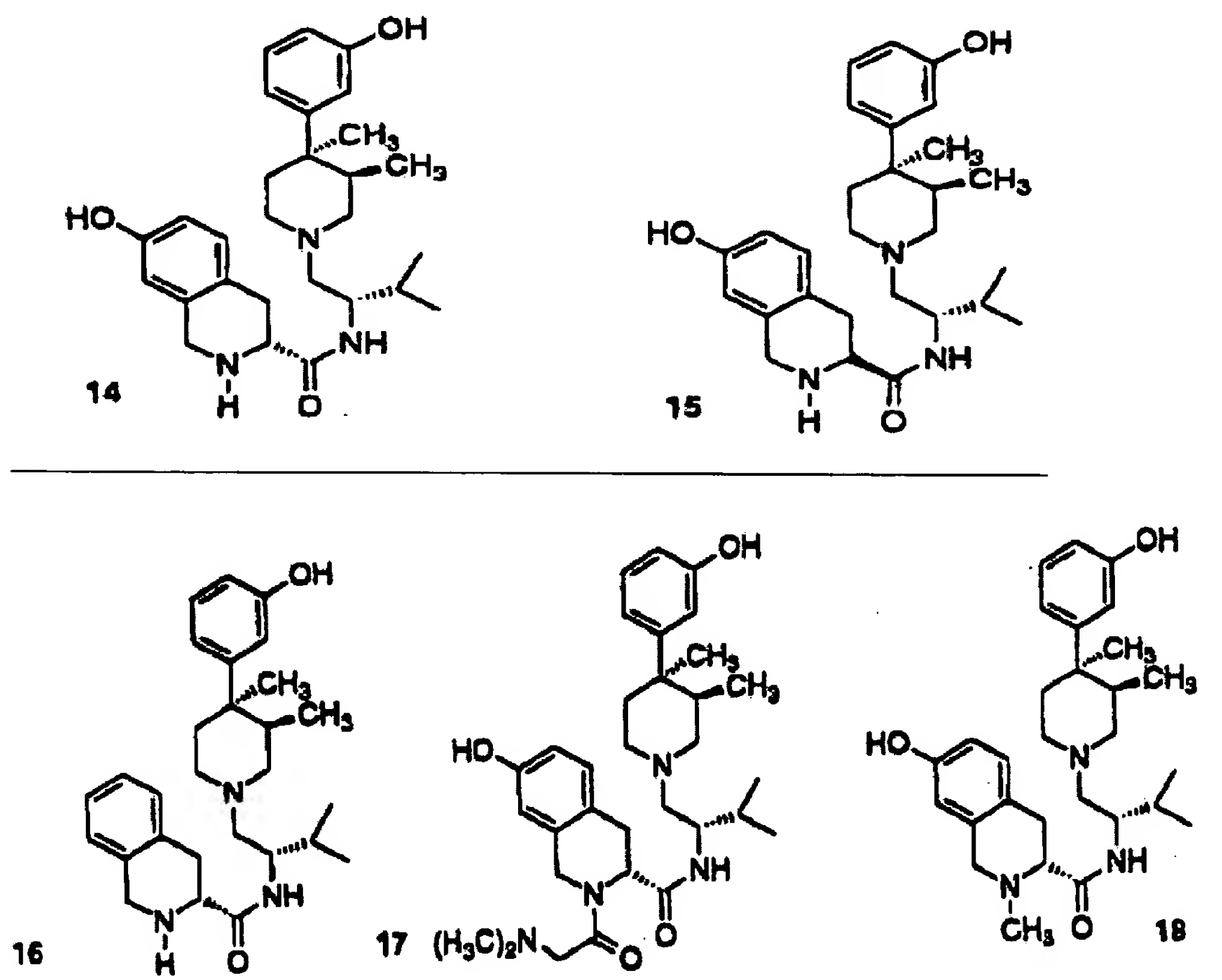
R_4 is C_{1-8} alkyl, or CO_2C_{2-8} alkyl, and the stereocenter adjacent to R_4 has a
configuration of (S);

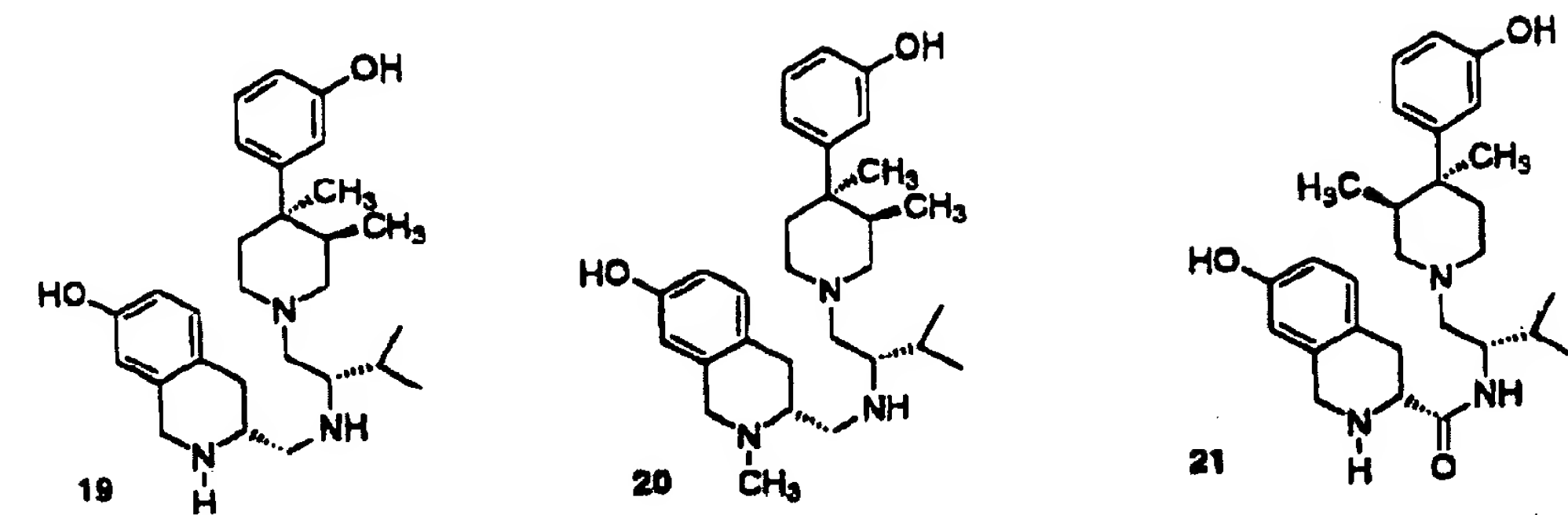
R_5 is H;

R_6 is a group having a formula selected from the group consisting of structures (a) and (b); and

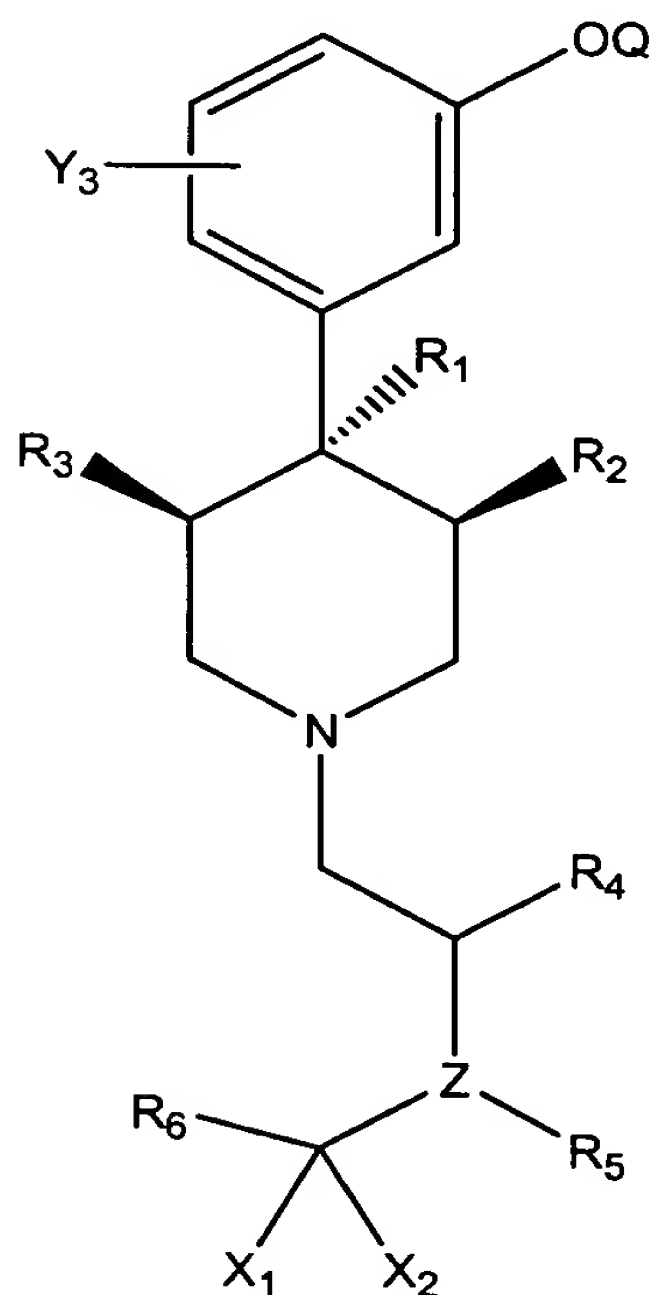
R_7 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 or $CH_2(CH_2)_nY_2$.

Claim 12 (Currently Amended) The kappa opioid receptor antagonist of claim 7, wherein said compound is a compound selected from formulae 14-21 of Fig. 1 as follows:





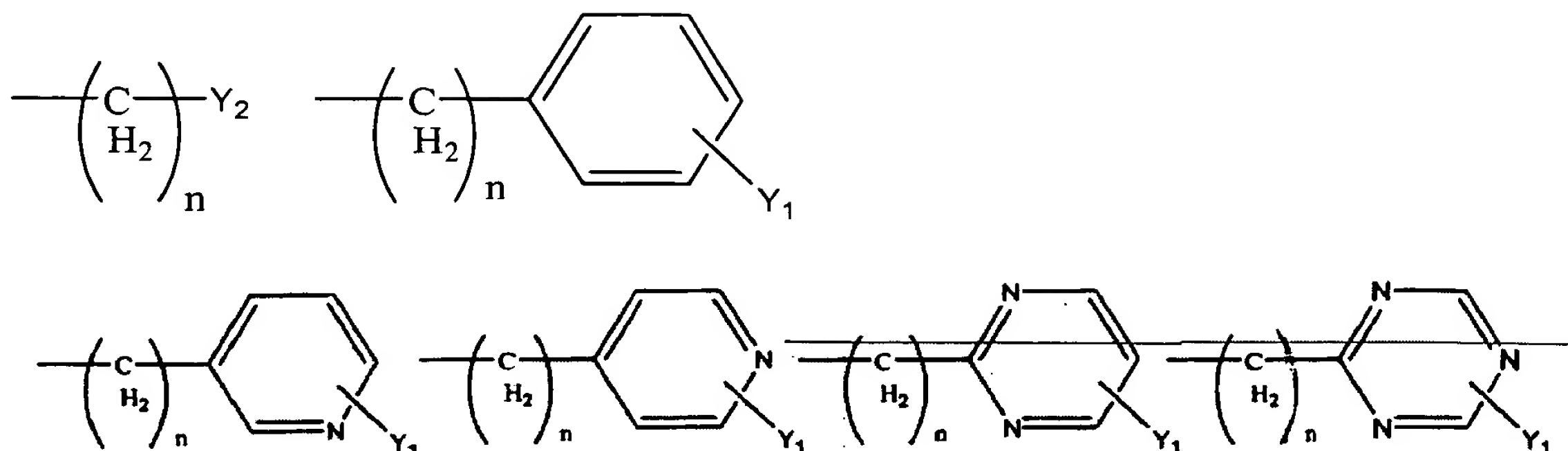
Claim 13 (Currently Amended) A pharmaceutical composition comprising:
 an effective amount of a kappa opioid receptor antagonist and a physiologically
 acceptable carrier, wherein the kappa opioid receptor antagonist is a compound of formula
 (I):



(I)

wherein Q is H or COC_{1-8} alkyl;

R_1 is C_{1-8} alkyl, or one of the following structures:



Y_1 is H, OH, Br, Cl, F, CN, CF_3 , NO_2 , N_3 , OR_8 , CO_2R_9 , C_{1-6} alkyl, $\text{NR}_{10}\text{R}_{11}$, NHCOR_{12} , $\text{NHCO}_2\text{R}_{12}$, $\text{CONR}_{13}\text{R}_{14}$, or $\text{CH}_2(\text{CH}_2)_n\text{Y}_2$;

Y_2 is H, CF_3 , CO_2R_9 , C_{1-6} alkyl, $\text{NR}_{10}\text{R}_{11}$, NHCOR_{12} , $\text{NHCO}_2\text{R}_{12}$, $\text{CONR}_{13}\text{R}_{14}$, CH_2OH , CH_2OR_8 , or COCH_2R_9 ;

Y_3 is H, OH, Br, Cl, F, CN, CF_3 , NO_2 , N_3 , OR_8 , CO_2R_9 , C_{1-6} alkyl, $\text{NR}_{10}\text{R}_{11}$, NHCOR_{12} , $\text{NHCO}_2\text{R}_{12}$, $\text{CONR}_{13}\text{R}_{14}$, or $\text{CH}_2(\text{CH}_2)_n\text{Y}_2$;

R_2 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl or CH_2aryl substituted by one or more groups Y_1 ;

R_3 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl or CH_2aryl substituted by one or more groups Y_1 ;

wherein R_2 and R_3 may be bonded together to form a C_{2-8} alkyl group;

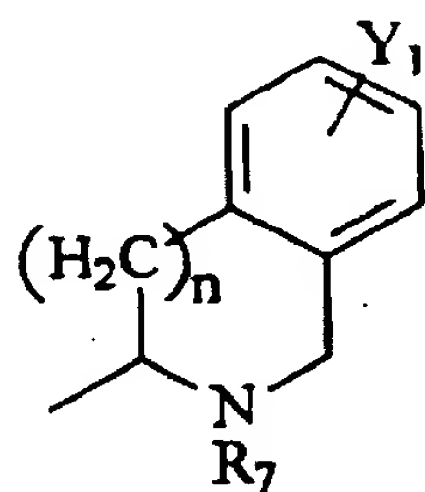
R_4 is hydrogen, C_{1-8} alkyl, $\text{CO}_2\text{C}_{1-8}$ alkylaryl substituted by one or more groups Y_1 , CH_2aryl substituted by one or more groups Y_1 , or $\text{CO}_2\text{C}_{1-8}$ alkyl;

Z is N, O or S; when Z is O or S, there is no R_5

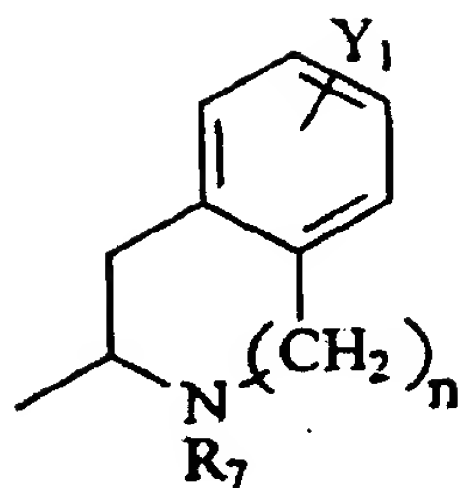
R_5 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, $\text{CH}_2\text{CO}_2\text{C}_{1-8}$ alkyl, $\text{CO}_2\text{C}_{1-8}$ alkyl or CH_2aryl substituted by one or more groups Y_1 ;

n is 0, 1, 2 or 3;

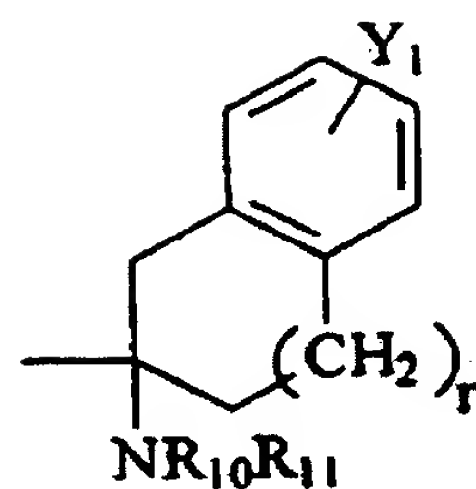
R_6 is a group selected from the group consisting of structures (a)-(w) and (cc)-(bbb):



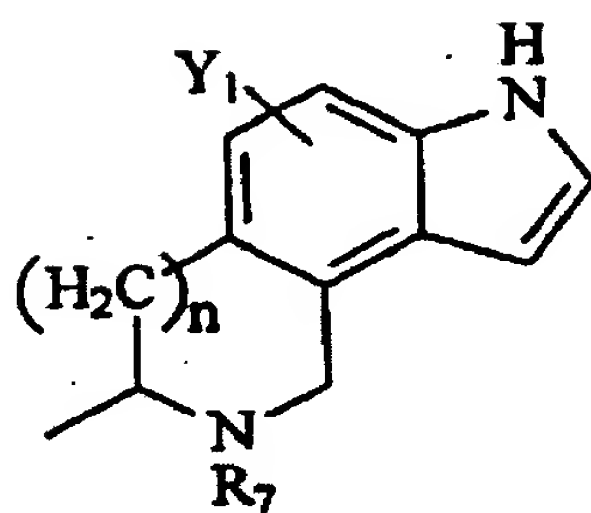
(a)



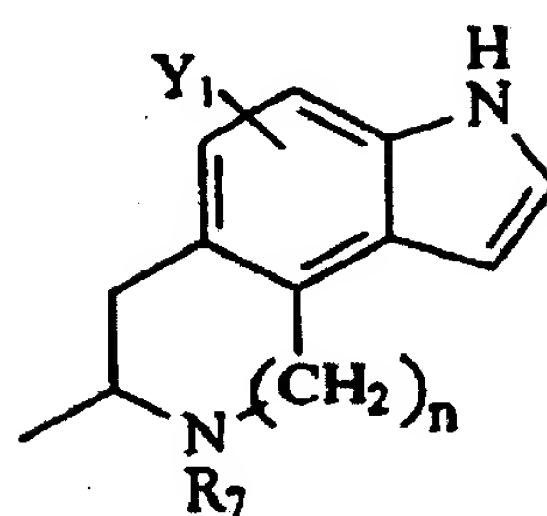
(b)



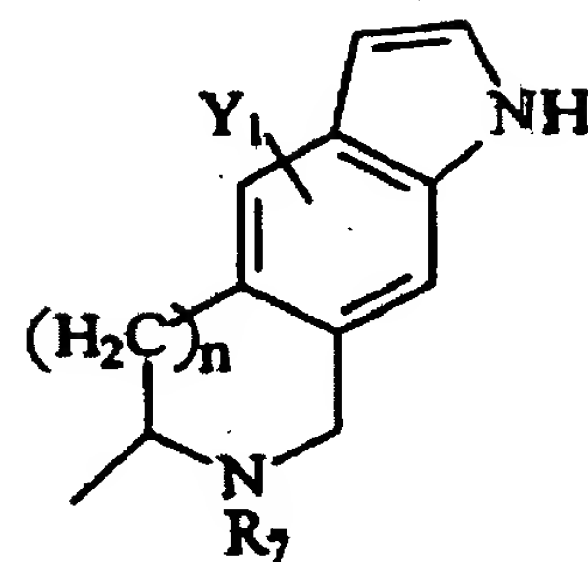
(c)



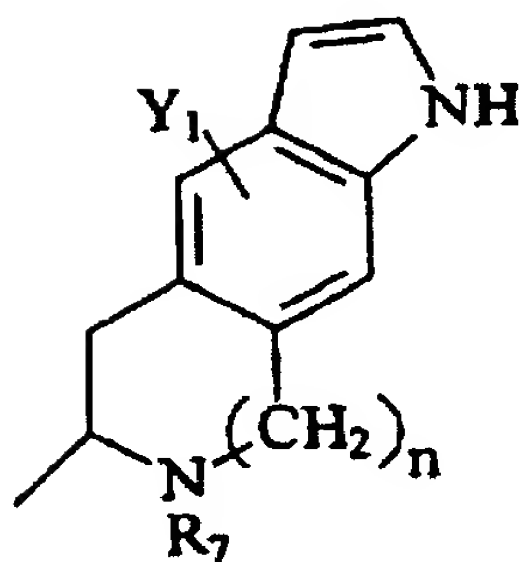
(d)



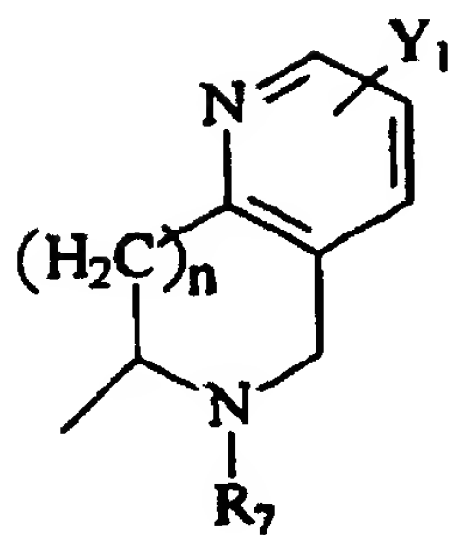
(e)



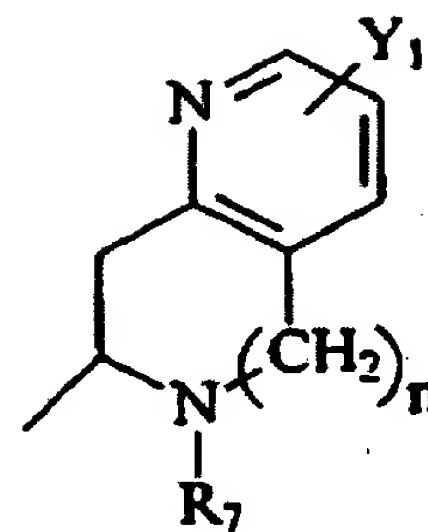
(f)



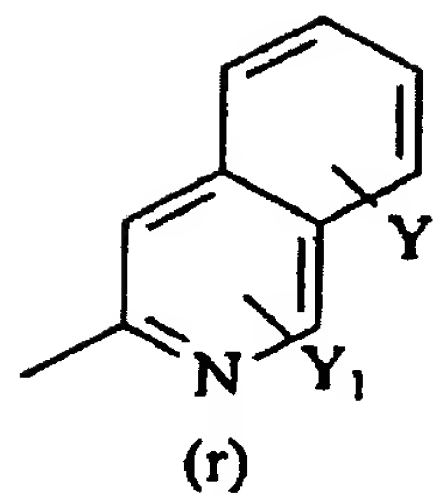
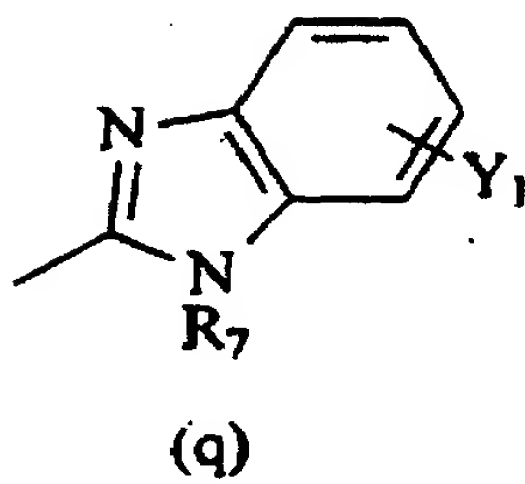
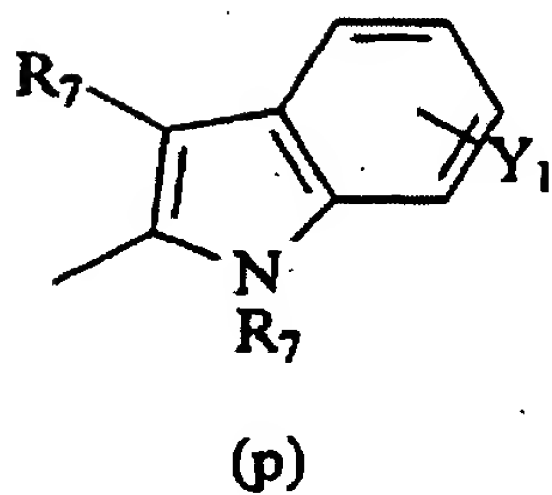
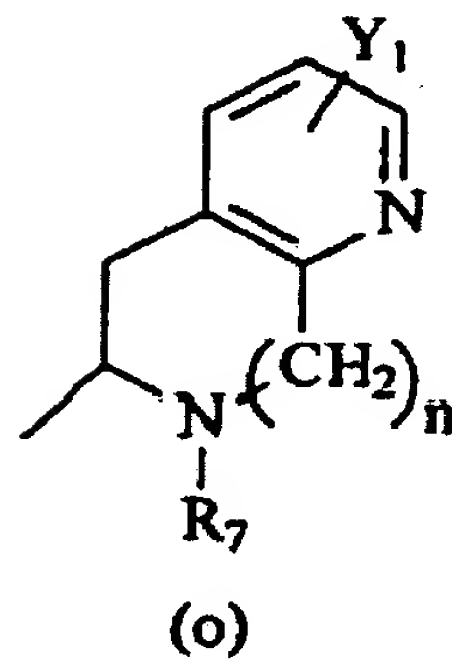
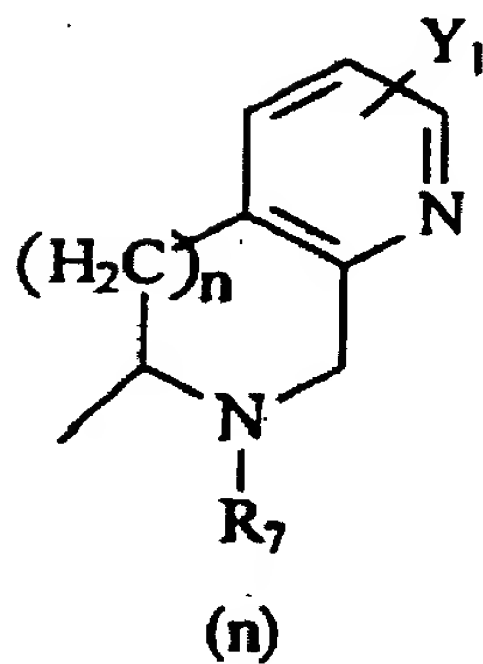
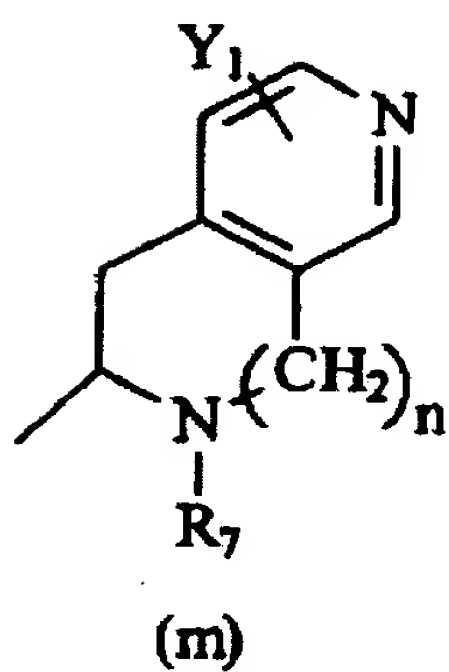
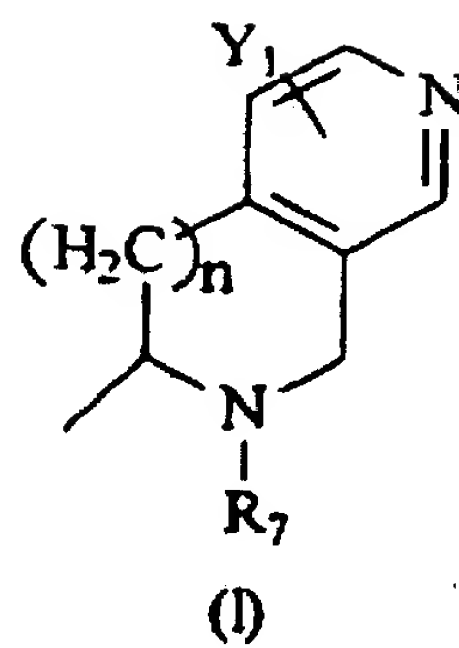
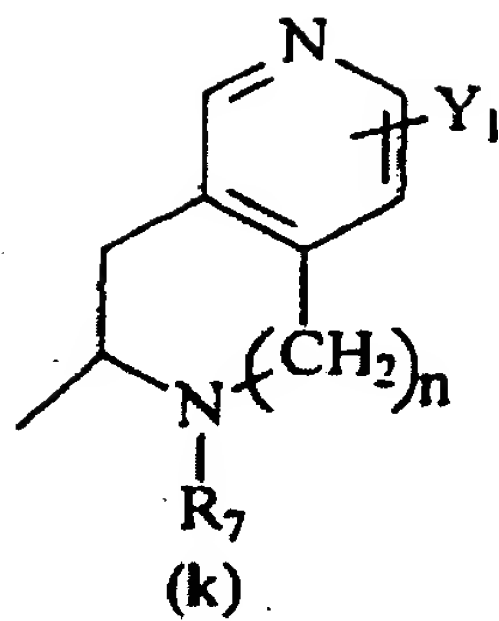
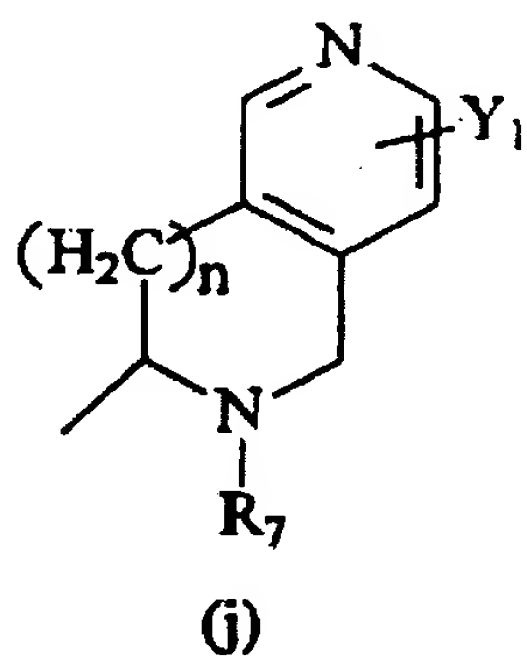
(g)

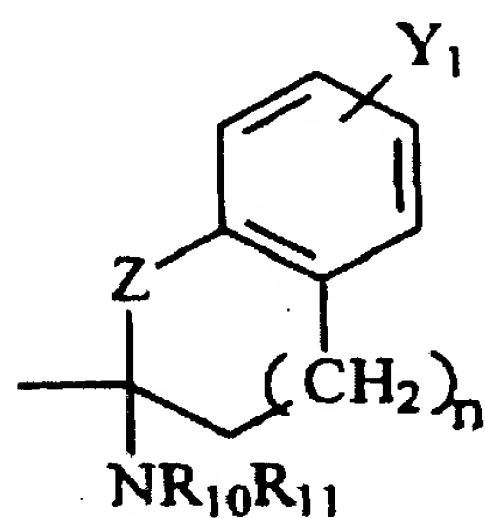


(h)

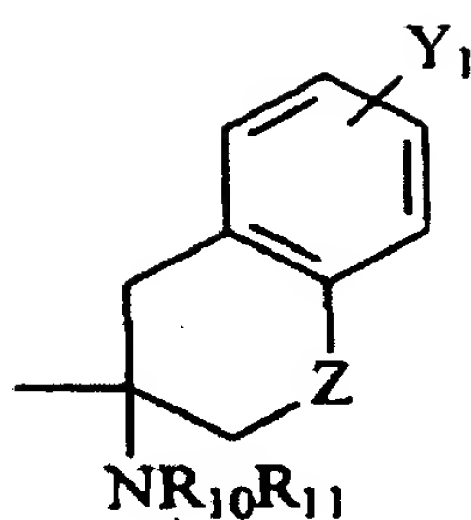


(i)

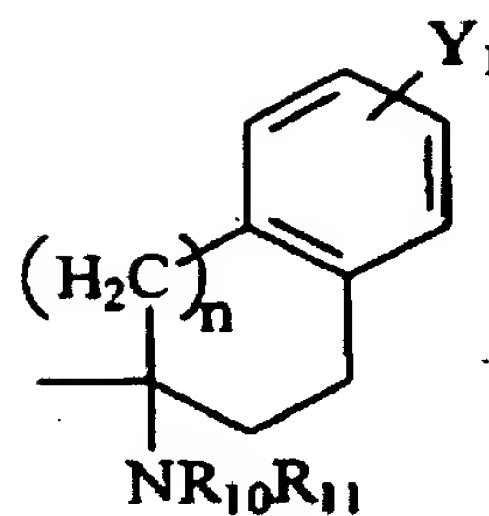




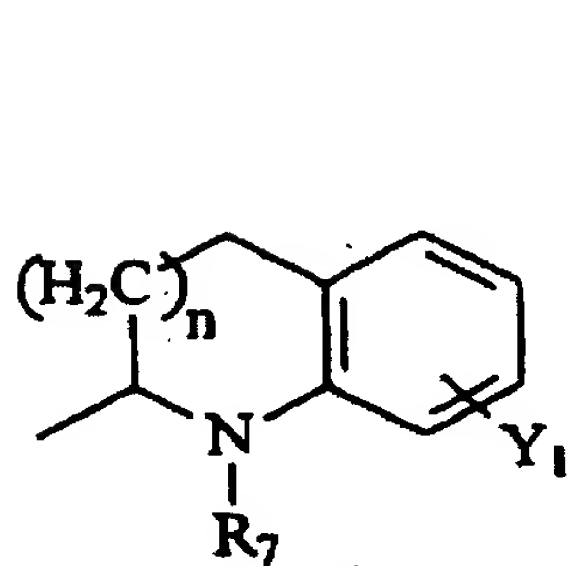
(s)



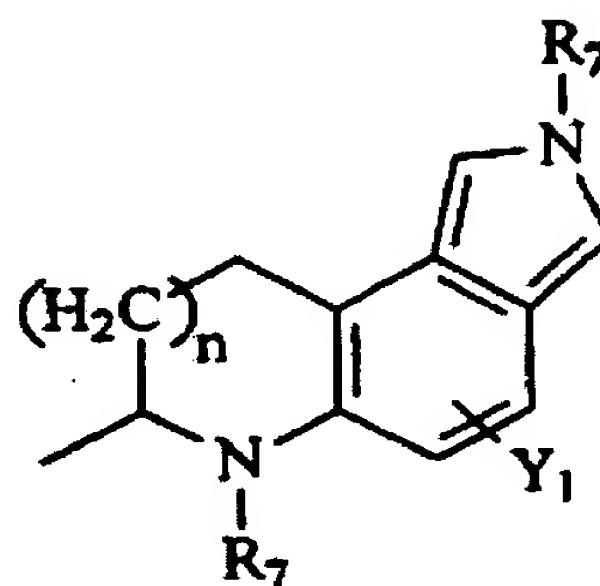
(t)



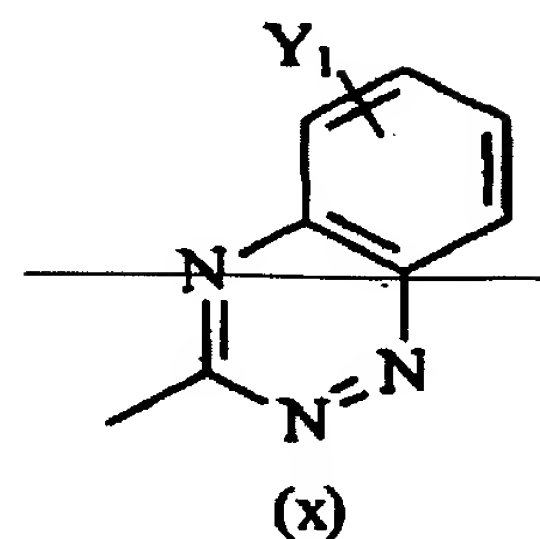
(u)



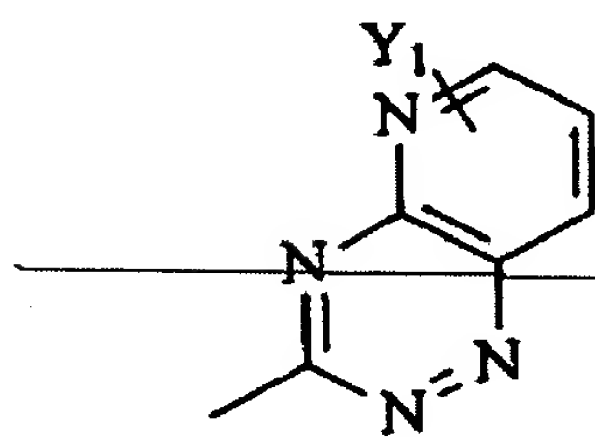
(v)



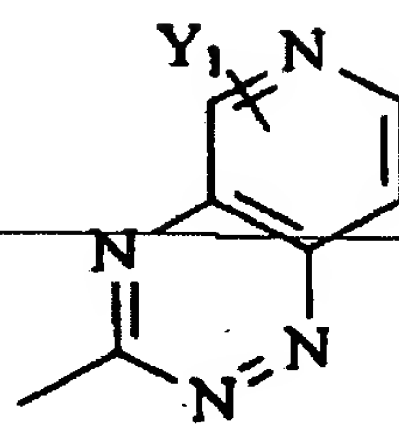
(w)



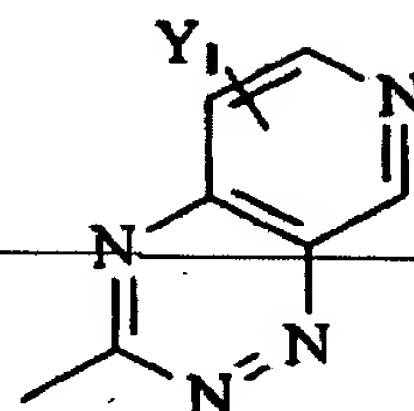
(x)



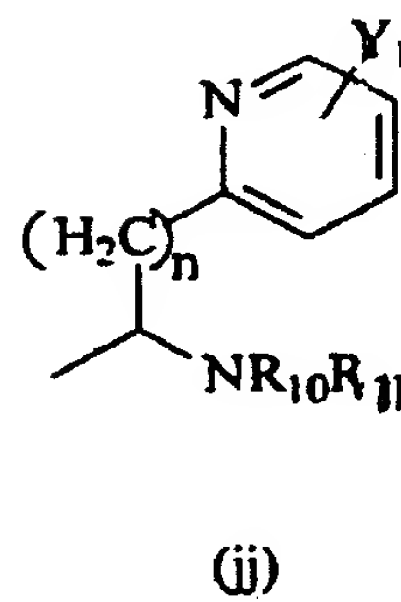
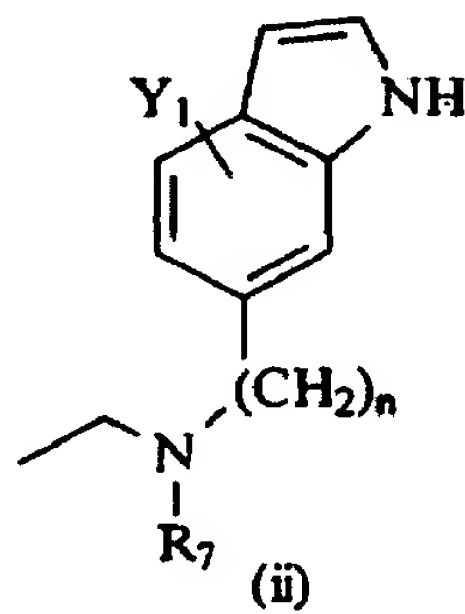
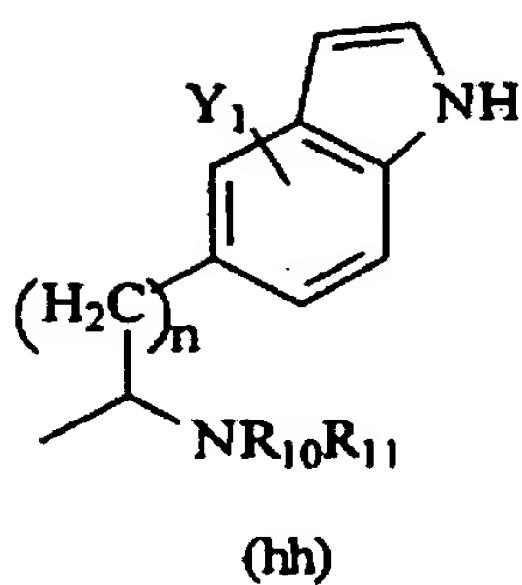
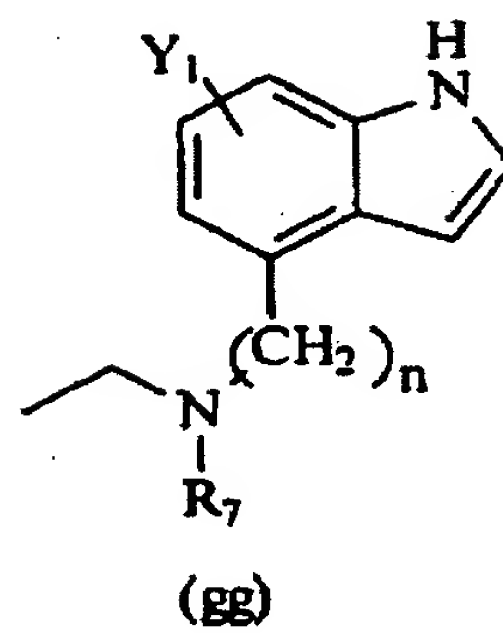
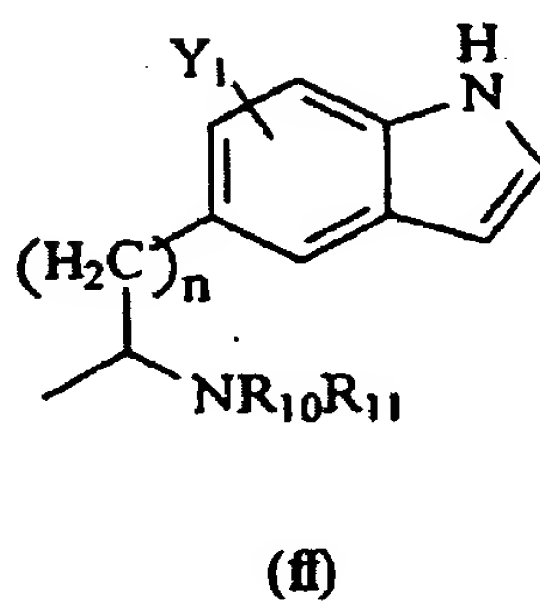
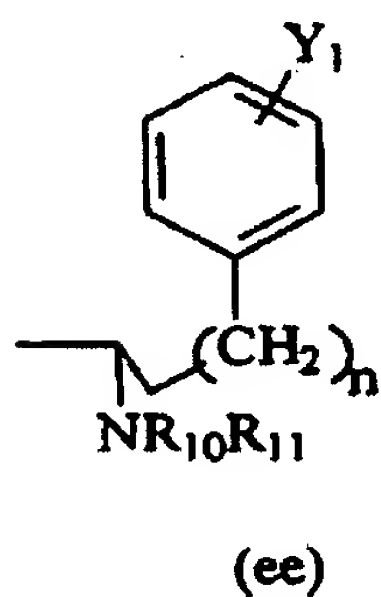
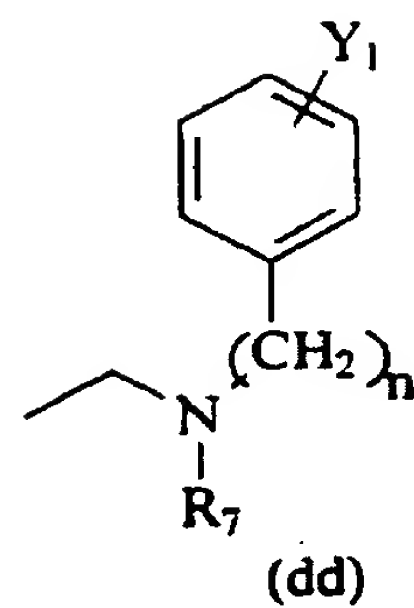
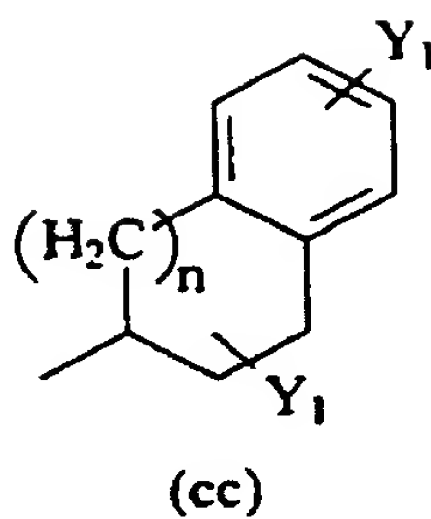
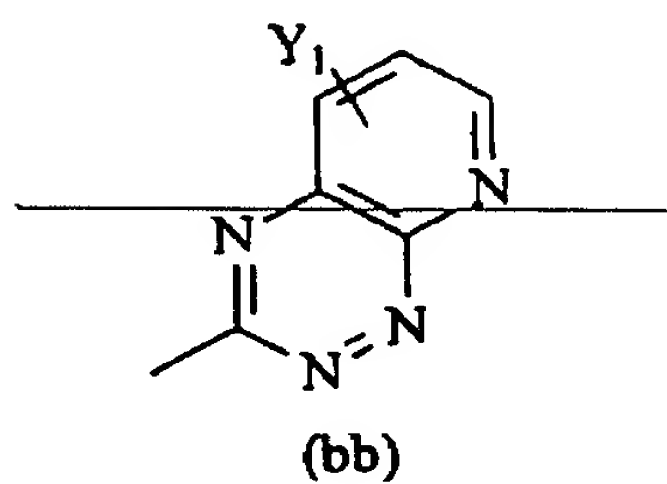
(y)

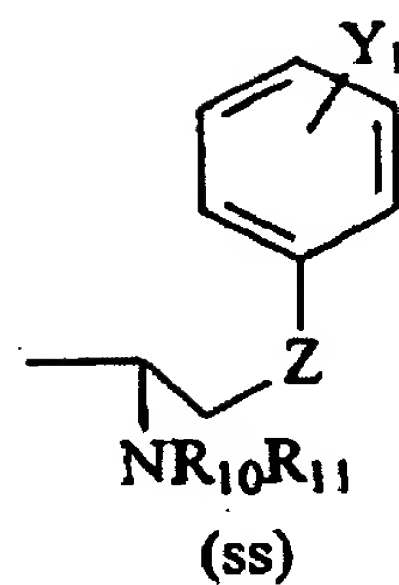
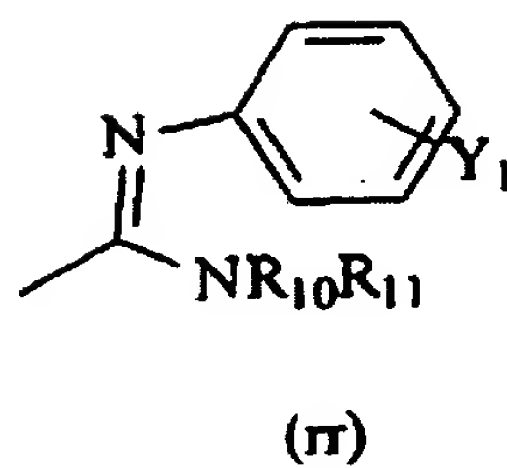
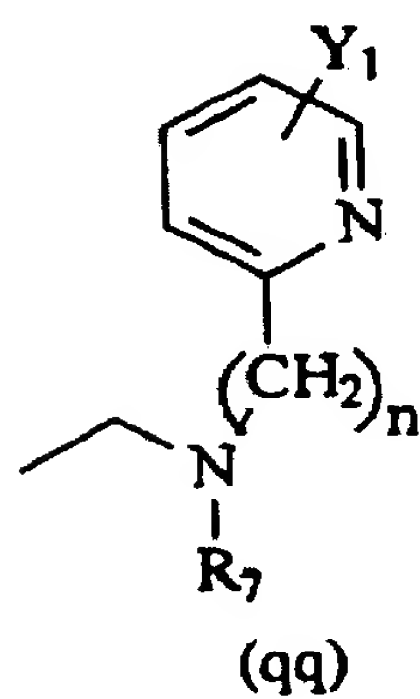
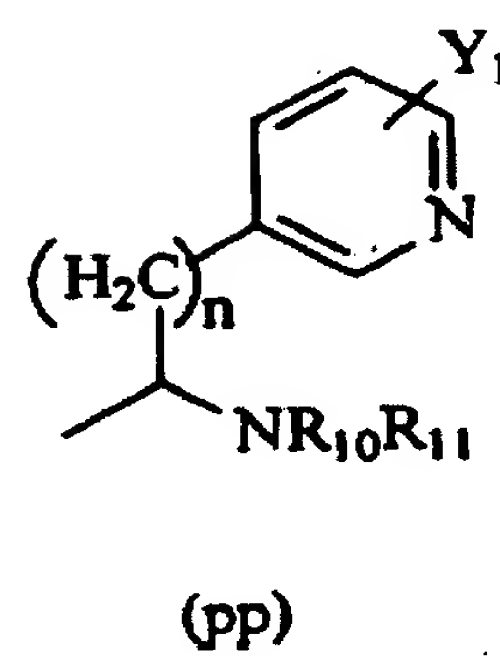
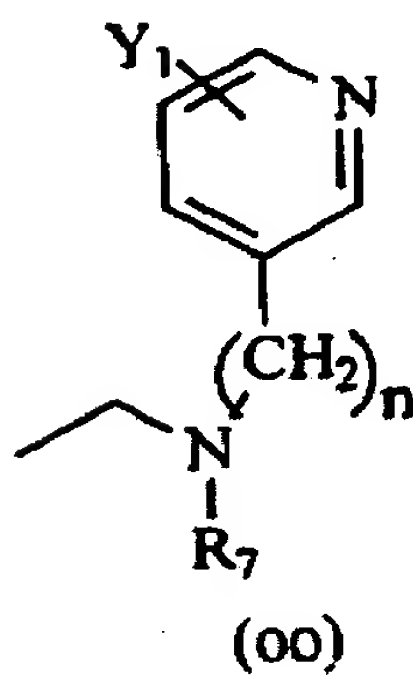
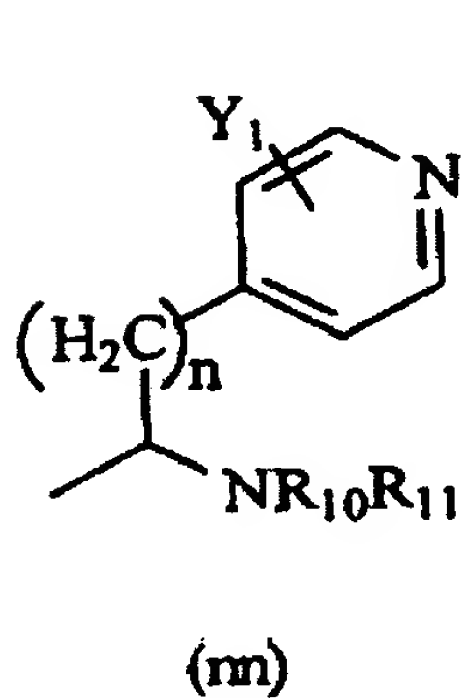
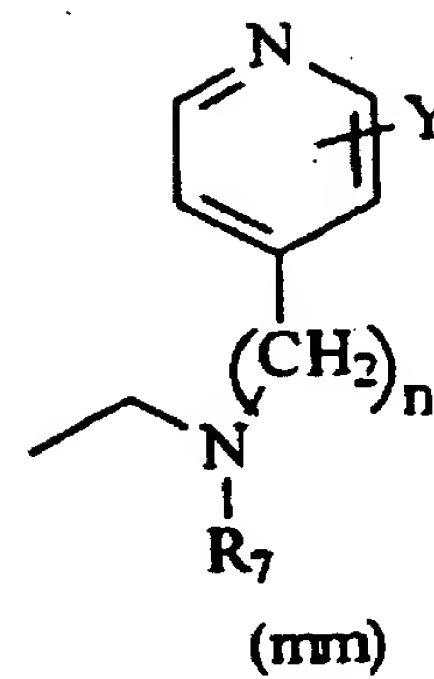
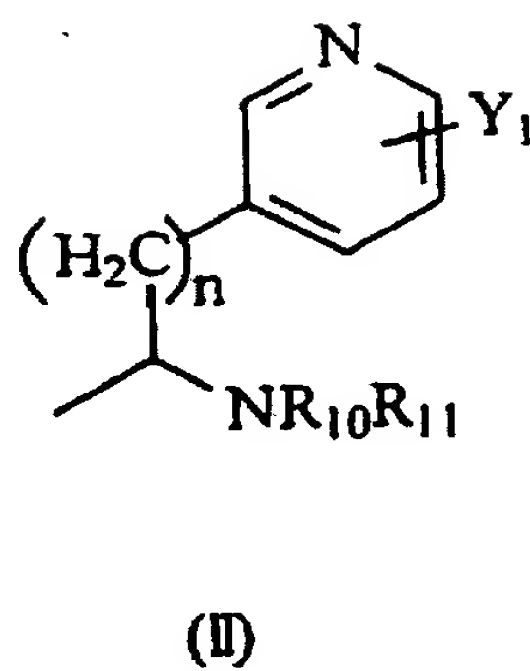
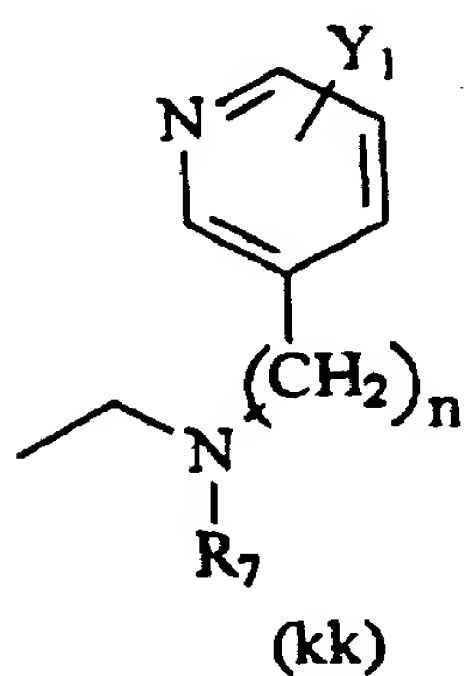


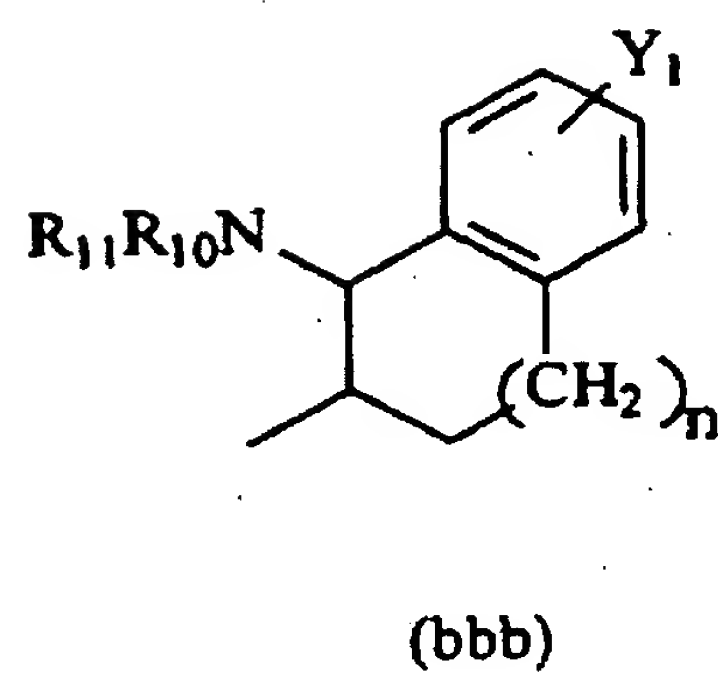
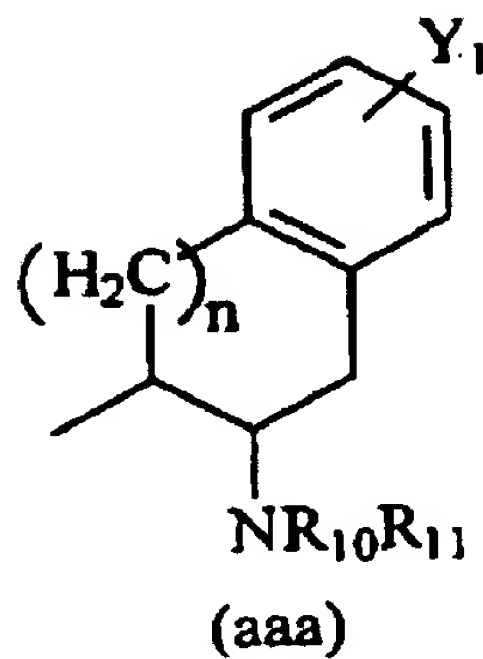
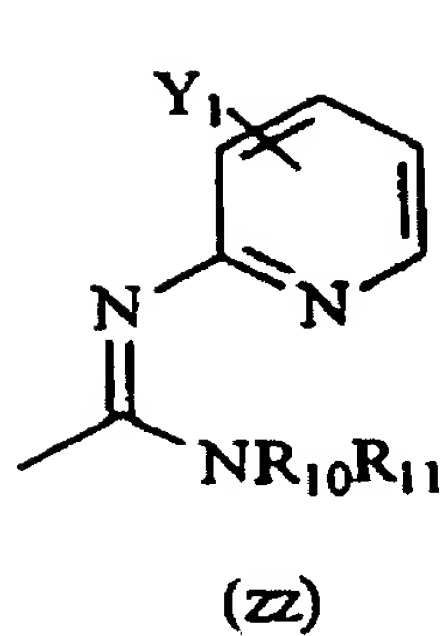
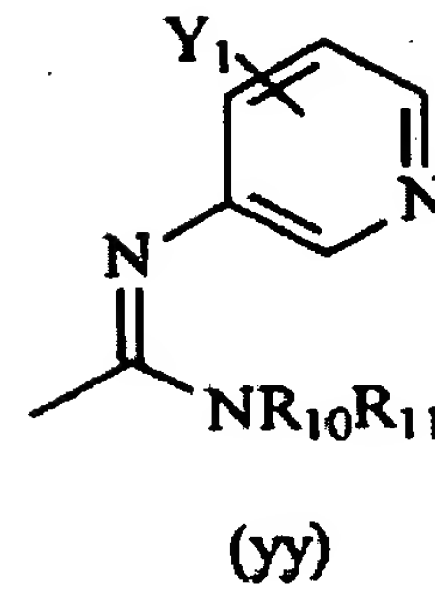
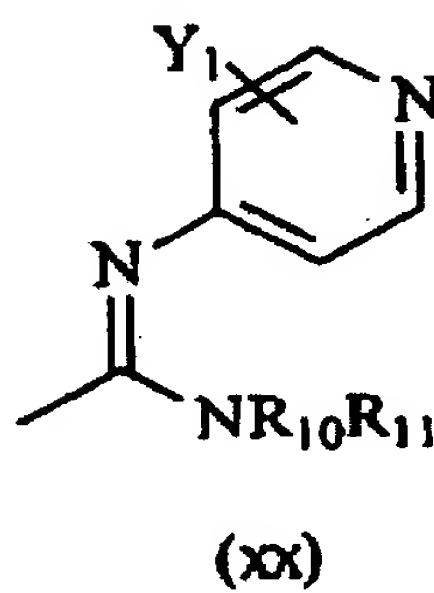
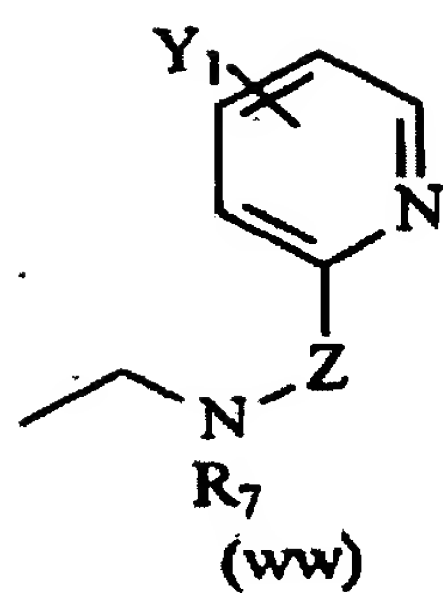
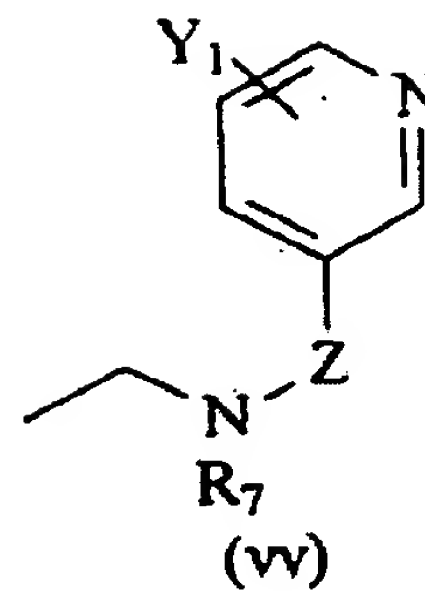
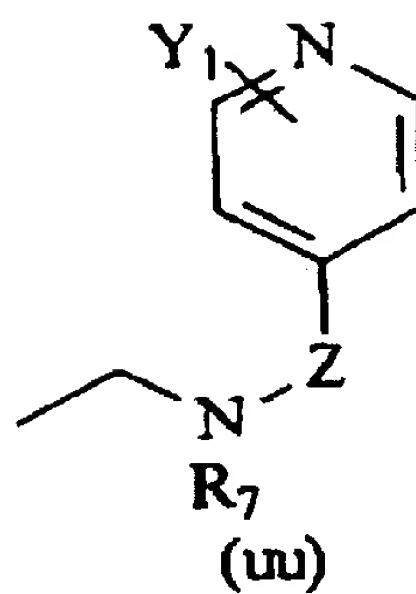
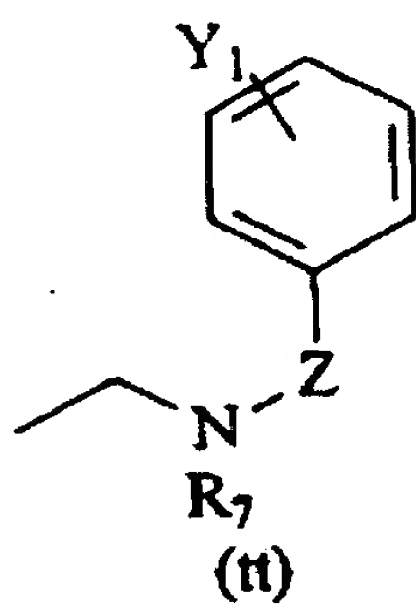
(z)



(aa)







X₁ is hydrogen, C₁₋₈ alkyl, C₃₋₈alkenyl, or C₃₋₈alkynyl;

X₂ is hydrogen, C₁₋₈alkyl, C₃₋₈alkenyl, or C₃₋₈alkynyl;

or X₁ and X₂ together form =O, =S, =NH;

R₇ is H, C₁₋₈alkyl, CH₂aryl substituted by one or more substituents Y₁, NR₁₀R₁₁,
NHCOR₁₂, NHCO₂R₁₃, CONR₁₄R₁₅, CH₂(CH₂)_nY₂, or C(=NH)NR₁₆R₁₇;

R₈ is H, C₁₋₈alkyl, CH₂ aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆ alkyl, or CH₂(CH₂)_nY₂' ; wherein Y₂' is H, CF₃, or C₁₋₆alkyl;

R₉ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆ alkyl, or CH₂(CH₂)_nY₂' ; wherein Y₂' is H, CF₃, or C₁₋₆alkyl;

R₁₀ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆ alkyl, or CH₂(CH₂)_nY₂' ; wherein Y₂' is H, CF₃, or C₁₋₆alkyl ;

R₁₁ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆ alkyl, or CH₂(CH₂)_nY₂' ; wherein Y₂' is H, CF₃, or C₁₋₆alkyl ;

R₁₂ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆ alkyl, or CH₂(CH₂)_nY₂' ; wherein Y₂' is H, CF₃, or C₁₋₆alkyl ;

R₁₃ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆ alkyl, or CH₂(CH₂)_nY₂' ; wherein Y₂' is H, CF₃, or C₁₋₆alkyl ;

R₁₄ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆ alkyl, or CH₂(CH₂)_nY₂' ; wherein Y₂' is H, CF₃, or C₁₋₆alkyl ;

R₁₅ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆ alkyl, or CH₂(CH₂)_nY₂' ; wherein Y₂' is H, CF₃, or C₁₋₆alkyl ;

R₁₆ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆ alkyl, or CH₂(CH₂)_nY₂' ; wherein Y₂' is H, CF₃, or C₁₋₆alkyl ; and

R₁₇ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents H, OH, Br, Cl, F,
CN, CF₃, NO₂, N₃, C₁₋₆ alkyl, or CH₂(CH₂)_nY₂' ; wherein Y₂' is H, CF₃, or C₁₋₆alkyl

or a pharmaceutically acceptable salt thereof.

Claim 14. (Currently Amended) The pharmaceutical composition of claim 13, wherein said kappa opioid receptor antagonist is a compound of formula (I), wherein R_1 , R_4 , R_5 , Y_1 , Y_2 , Z , n , X_1 , X_2 , and R_7 - R_{17} are as in Claim 13;

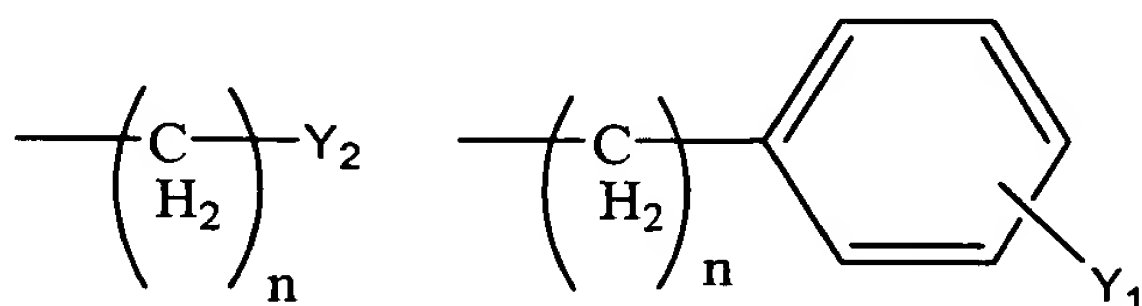
Y_3 is H;

R_2 and R_3 are each, independently, H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, or CH_2 aryl substituted by one or more substituents Y_1 ; and

R_6 is a group having a formula selected from the group consisting of structures (a)-(w) and (cc).

Claim 15. (Previously Presented) The pharmaceutical composition of claim 13, wherein said kappa opioid receptor antagonist is a compound of formula (1), wherein Y_1 , Y_2 , R_4 , R_5 , Z , n , X_1 , X_2 and R_8 - R_{15} are as in Claim 13;

R_1 is C_{1-8} alkyl, or one of the following structures:



Y_3 is H;

R_2 and R_3 are each, independently, H or C_{1-8} alkyl, wherein R_2 and R_3 cannot both be H at the same time;

R_6 is a formula selected from the structures (a)-(r) shown above; and

R_7 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , $NR_{10}R_{11}$, $NHCO R_{12}$, $NHCO_2 R_{13}$, $CONR_{14}R_{15}$, or $CH_2(CH_2)_n Y_2$.

Claim 16. (Previously Presented) The pharmaceutical composition of claim 13, wherein said kappa opioid receptor antagonist is a compound of formula (I), wherein Y_1 , Z , n , X_1 , X_2 and R_8 - R_{15} are as noted- above in Claim 13;

R_1 is C_{1-8} alkyl;

Y_2 is H, CF_3 , CO_2R_9 , C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, CH_2OH , CH_2OR_8 , or $COCH_2R_9$;

Y_3 is H;

R_2 and R_3 are each, independently, H or methyl, wherein R_2 and R_3 cannot both be H at the same time;

R_4 is H, C_{1-8} alkyl, CO_2C_{1-8} alkyl, or CH_2 aryl substituted by one or more substituents Y_1 and the stereocenter adjacent to R_4 is in an (S) configuration;

R_5 is H, C_{1-8} alkyl, $CH_2CO_2C_{1-8}$ alkyl;

R_6 is a group having a formula selected from the group consisting of structures (a)-(c) and (h)-(o); and

R_7 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{13}$, $CONR_{14}R_{15}$, or $CH_2(CH_2)_nY_2$.

Claim 17. (Previously Presented) The pharmaceutical composition of claim 13, wherein said kappa opioid receptor antagonist is a compound of formula (1), wherein Y_1 , Z , n , X_1 , X_2 and R_8 - R_{14} are as in Claim 13;

R_1 is methyl,

Y_2 is H, CF_3 , CO_2R_9 , C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, CH_2OH , CH_2OR_8 , or $COCH_2R_9$;

Y_3 is H;

R_2 and R_3 are each H or methyl, such that when R_2 is H, R_3 is methyl and vice versa;

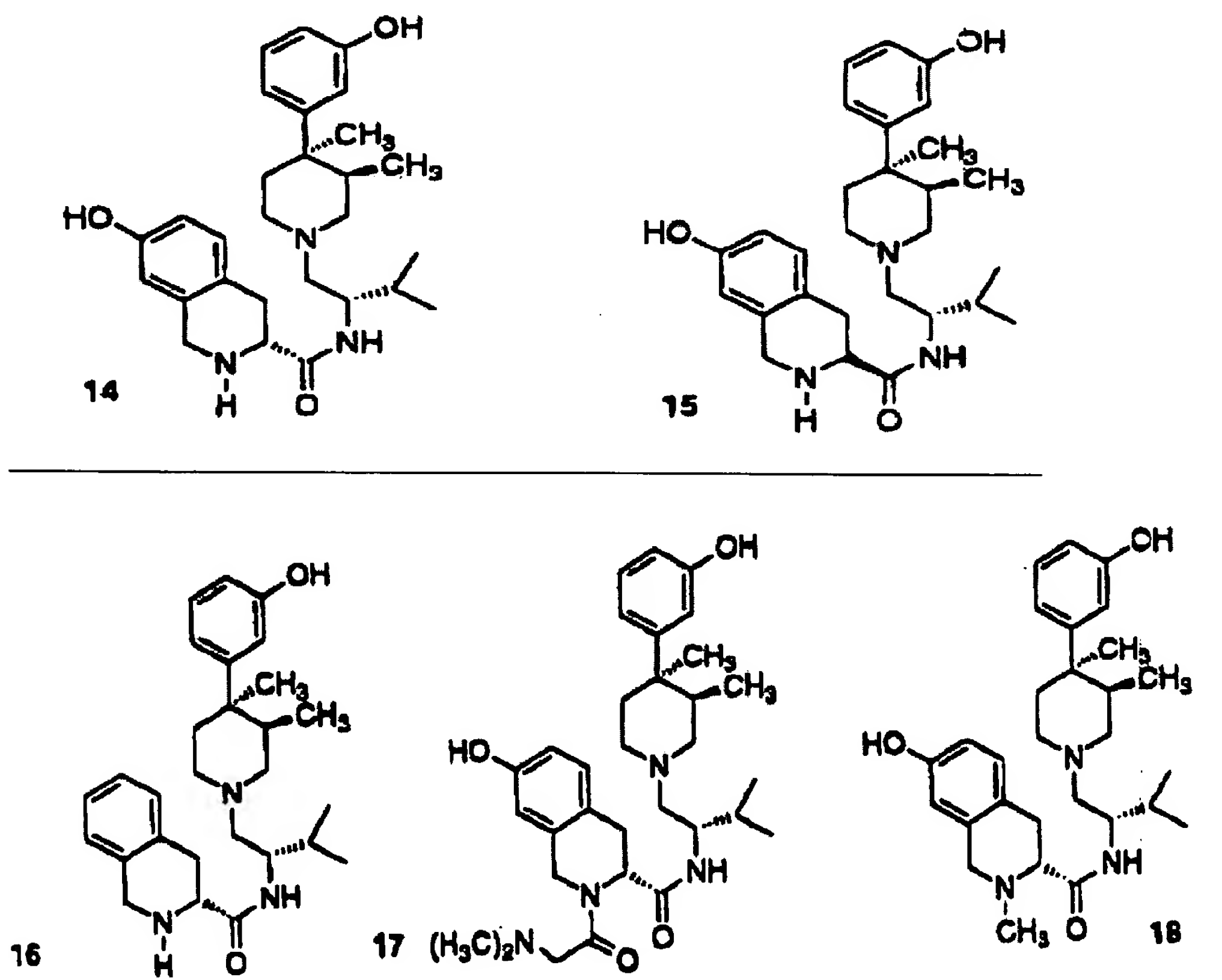
R_4 is C_{1-8} alkyl, or CO_2C_{1-8} alkyl, and the stereocenter adjacent to R_4 has a configuration of (S);

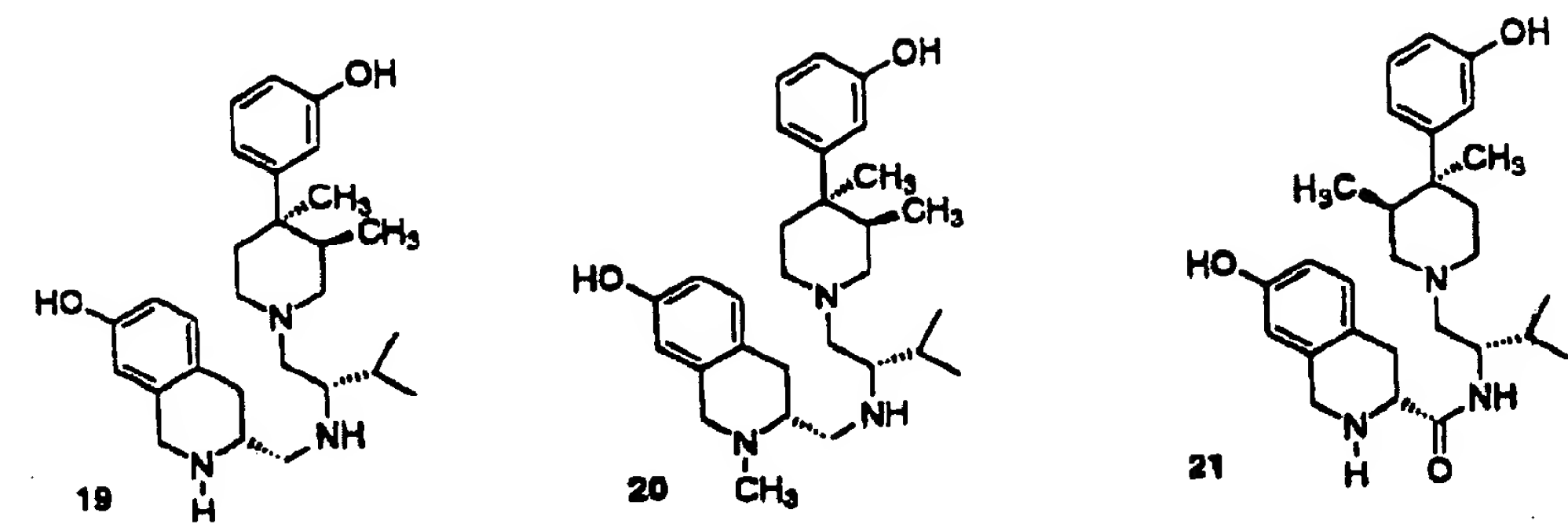
R_5 is H;

R_6 is a group having a formula selected from the group consisting of structures (a) and (b); and

R_7 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y, or $CH_2(CH_2)_nY_2$.

Claim 18. (Currently Amended) The pharmaceutical composition of claim 13, wherein said kappa opioid receptor antagonist is a compound selected from formulae 14-21 of Fig. 1 as follows:



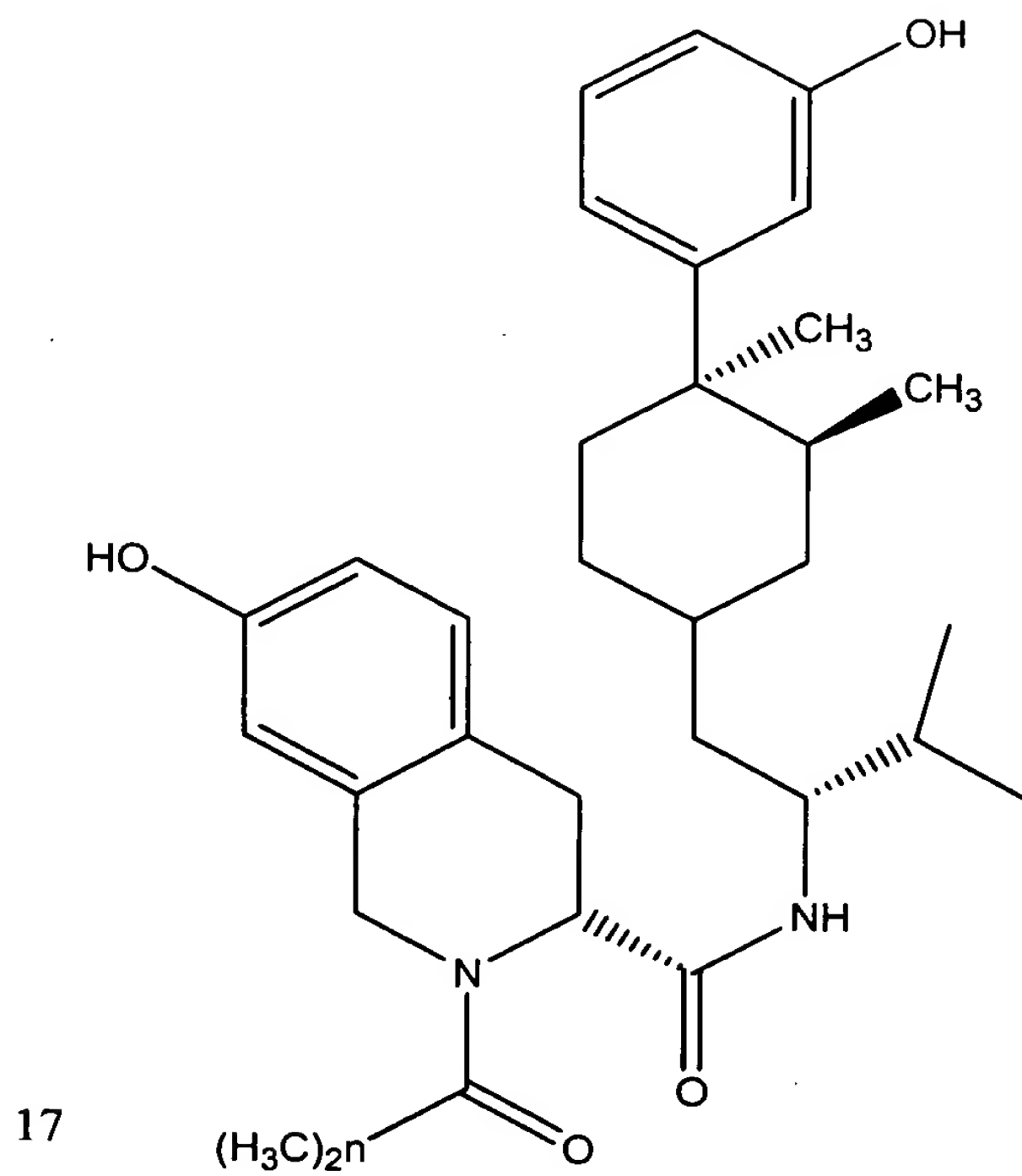


Claim 19. (Original) The pharmaceutical composition of claim 13, wherein said composition is an injectable composition.

Claim 20. (Original) The pharmaceutical composition of claim 13, wherein said composition is an orally administrable composition.

Claim 21. (Original) The pharmaceutical composition of claim 20, wherein said orally administrable composition is in a form selected from the group consisting of tablets, capsules, troches, powders, solutions, dispersions, emulsions and suspensions.

Claim 22. (Previously Presented) The kappa opioid receptor antagonist according to Claim 7, having the chemical formula:



Claim 23. (Cancelled)

Claim 24. (Cancelled)

Claim 25. (Cancelled)